CB 17/82/01

NCI/ICRDB/CB17 82/01

PB82-931801

# ICRDB CANCERGRAM

# IMMUNOBIOLOGY AND CANCER

## Identification and Characterization of Immune Cells

SERIES CB17 No. 82/01

JANUARY, 1982

This Cancergram is a service of the INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM of the U.S. National Cancer Institute. Every few weeks, an updated Cancergram containing abstracts of selected cancer-related articles recently published in more than 3000 journals, and dealing with the topic indicated by the above title, is sent to researchers working in this area. These researchers are identified on the basis of the description of their current research project that has been submitted to the ICRDB Program, directly or via granting agencies.

This Cancergram is prepared by the Cancer Information Dissemination and Analysis Center (CIDAC) for Virology, Immunology, and Biology. ***If this Cancergram is useful and valuable, please send your comments to the CIDAC address below, since future editions depend on user satisfaction and user needs:***

CIDAC FOR VIROLOGY, IMMUNOLOGY, AND BIOLOGY
SCIENCE INFORMATION SERVICES
FRANKLIN INSTITUTE RESEARCH LABORATORIES
20TH AND RACE STREETS
PHILADELPHIA, PA 19103

NEWARK PUBLIC LIBRARY

FEB 1 1982

U. S. GOVT. PUBS.
DEPOSITORY 376

*In this issue:*


- CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS..... 1-12
- DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS..... 13-28
- LYMPHOCYTE AND DIFFERENTIATION ANTIGENS..... 29-40
- CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION..... 41-53
- EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS..... 54-73
- OTHER RELATED STUDIES..... 74-87


## CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS

### 1. CYTOCHEMISTRY AND MEMBRANE MARKERS IN ACUTE LYMPHATIC LEUKAEMIA (ALL).

Huhn D, Thiel E, Rodt H, Andreewa P
Medizinische Klinik III, Grosshadern, Marchioninistr. 15, D-8000 Munchen 70, W. Germany
Scand J Haematol; 26(4):311-320 1981

One hundred thirty-six patients suffering from ALL were subdivided into 5 subtypes (C-ALL, C/T-ALL, pre-T-ALL, B-ALL) according to rosetting tests and using specific antisera directed against membrane antigens. In addition, leukemic blasts of all patients were investigated according to morphological and cytochemical criteria. In APh and ANAE, indices and the percentages of cases showing a granular staining pattern were high in pre-T- and in T-ALL, but low in C/T- and in C-ALL. PAS-staining, conversely, was more pronounced in C/T- and C-ALL. APh proved to be more discriminative for recognition of the T- and Pre-T-ALL subgroups than ANAE, but ANAE-cytochemistry may be useful to detect contaminat-

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service • National Institutes of Health • National Cancer Institute

HE20.3173/2:

ing normal T-lymphocytes in ALL. Receptors for C3 were more frequent in C- and in T-ALL than in C/T- and in pre-T-ALL, receptors for Fc were distributed equally among all subtypes. Positivity of C3-and Fc-receptors was not correlated with cytochemical results. Morphological criteria were not sufficient for subclassification of ALL; the combination of APh- and PAS-staining, however, is valuable to differentiate between C-subgroups and T-subgroups. (Author abstract) (36 Refs)

## 2. MONOCLONAL ANTIBODY OKT-9 RECOGNIZES THE RECEPTOR FOR TRANSFERRIN ON HUMAN ACUTE LYMPHOCYTIC LEUKEMIA CELLS.

Goding JW, Burns GF
Walter and Eliza Hall Inst. Medical Res., Post Office, Royal Melbourne Hosp., Victoria, 3050, Australia
J Immunol; 127(3):1256-1258 1981

The monoclonal antibody OKT-9 recognizes a surface protein of human lymphocytes that consists of a disulfide bonded homodimer of mol wt 200,000 intact and 95,000 reduced. A similar protein is precipitated by transferrin-agarose, but not by agarose alone. Peptide mapping by limited proteolysis shows that the proteins precipitated by OKT-9 antibodies and transferrin-agarose are homologous. It is concluded that OKT-9 antibodies recognize the transferrin receptor. Expression of receptors for transferrin may be useful as a marker for activated of dividing cells. (Author abstract) (21 Refs)

## 3. ACUTE LYMPHOCYTIC LEUKEMIA AND COMPLEMENT RECEPTORS (A STUDY OF 45 CASES).

De Rossi G, Gugliemi C, Lopez M, Pasqualetti D, Mandelli F
Cattedra di Ematologia, Universita degli Studi di Roma, Via Arno 62, 00198 Roma, Italy
Ric Clin Lab; 11(2):139-143 1981

The relationship between the expression of complement receptors (C3R) and the expression of sheep erythrocyte receptors (ER) and surface membrane immunoglobulins (SmIg) was studied in 45 patients with acute lymphocytic leukemia (1-47 yr old) (ALL). Of 45 patients, 34 were at the onset of ALL, 9 were in the first relapse, and 2 were at onset and in the first relapse. C3R was constantly associated with SmIg (B cell ALL); C3R was frequently but not always associated with ER (T cell ALL). In three patients, C3R was not associated either with SmIg or with ER. (20 Refs)

## 4. REACTIVITY OF ANTISERA TO ANTIGENS OF C-TYPE VIRUSES WITH LEUCOCYTES FROM PATIENTS WITH ACUTE LEUKAEMIA.

Pullen S, Hersey P
(c/o Hersey) Kanematsu Memorial Inst., Sydney Hosp., Macquarie St., Sydney, Australia 2000
Pathology; 13(2):289-298 1981

A number of previous studies have suggested that certain C-type viruses from non -human primates are associated with acute leukemia in humans. The present study sought to examine this association furtner by detection of antigens related to these viruses on the surface of acute leukemia cells. Antisera against the whole viruses or the major internal protein of simian sarcoma, endogenous baboon and Rauscher viruses were tested against mononuclear cells from patients with acute leukemia at various stages of their disease in 51Cr release WBC dependent cytotoxic assays. A high proportion of the patients had antigens related to these viruses detectable on their blood WBC at some stage in their disease whereas with one exception blood WBC from non-leukemic subjects did not. The expression of these antigens did not show a close relation to the number of blast cells in blood detected on morphological grounds. Antigens related to the non-human primate viruses were detected on mononuclear cells from bone marrow samples of several non-leukemic patients which indicated they were not specifically associated with leukemia. Antigens related to the Rauscher virus were detected on cells of practically all bone marrow samples tested. These results suggest that assays to detect these antigens would be of limited usefulness to monitor disease activity in patients with acute leukemia. Their expression on blood WBC however appeared strongly associated with acute leukemia and further studies to assess the prognostic and epidemiological significance of detection of these antigens appears warranted. (Author abstract) (16 Refs)

## 5. A NOVEL HUMAN T CELL ANTIGEN PREFERENTIALLY EXPRESSED ON MATURE T CELLS AND SHARED BY BOTH WELL AND POORLY DIFFERENTIATED B CELL LEUKEMIAS AND LYMPHOMAS.

Kamoun M, Kadin ME, Martin PJ, Nettleton J, Hansen JA
Dept. Lab. Medicine, Univ. Washington SB-10, Seattle, WA, 98195
J Immunol; 127(3):987-991 1981

A new lymphocyte differentiation antigen shared by all normal T cells and some malignant B cells was defined by a monoclonal antibody designated 12.1. This antibody reacted with all peripheral blood T cells but not with normal B cells and B cell lines. Analysis with a fluorescence activated cell sorter showed that the expression of 12.1 antigen changes during T cell maturation. Most thymocytes, blasts of acute T cell leukemia, and cells from established leukemic T cell lines bear a small amount of 12.1 antigen. In contrast the majority of peripheral blood T cells, activated T cells, and leukemic T cells of the Sezary syndrome bear a large amount of 12.1 antigen. Unexpectedly, antibody 12.1 reacted with leukemic cells from most patients with B-type chronic lymphocytic leukemia (CLL) and some patients with lymphosarcoma cell leukemia (LSCL). Among these leukemias, expression of the 12.1 antigen was not correlated with the stage of B cell maturation, with the amount of surface immunoglobulin on the cells, or with the presence or absence of monoclonal gammopathy. In a comparative serologic analysis the antigen defined by antibody 12.1 was distinct from the p67 T cell antigen (defined by monoclonal antibody 10.2) that is also known to be expressed by B-type CLL cells. (Author abstract) (22 Refs)

## 6. ANALYSIS OF CELL-SURFACE ANTIGEN OF HAIRY CELL LEUKEMIA (HCL).

Ogasawara M, Ishii Y, Kikuchi K, Aikawa K, Mikuni C
First Dept. Pathology, Sapporo Medical Coll., Sapporo-shi, Hokkaido, 060, Japan
Igaku Ayumi; 116(1):29-31 1981

One patient with cell surface Ig-positive HCL and another patient with HCL shown to have B cell markers by immunoprecipitation with anti-HCG and anti-B serum were seen. An antiserum specific for hairy cells (AHCS) was obtained by immunizing rabbits with 2 x 10(7) hairy cells iv. The absorbed AHCS for both patients diluted 80-160x produced 100% fluorescein isothiocyanate-stained cells, but peripheral blood (T, B cells) and the two B-cell lymphoid leukemias were not responsive. Some tonsil B cells responded with fluorescence of 12-27%, but no T cells responded. Various leukemia cells other than the hairy cells barely responded to the lymphocytes, nor did they respond to the granulocyte or mono-

cyte leukemia cells. The unabsorbed antiserum had four major peaks, with mol wt of 110,000-120,000, 94,000-96,000, 48,000-50,000, and 30,000-34,000 for I, II, III, and IV. In the absorbed AHCS, peaks II and IV disappeared, leaving only I and II. The antigen at peak III is considered to differ from histocompatibility antigen (HLA) because it is not absorbed by anti-HLA or anti-beta2m. This antigen is considered to be the one that is differentiated from that of B cells which characterizes the hairy cell. The antigen at peak IV was also obtained by adding anti-B serum to the B cell lysates and the peak IV antigen that disappeared was considered to be an Ia-like antigen on the hairy cell. Antisera obtained from the two HCL patients were shown to recognize the same antigen. (Author abstract) (12 Refs) (In JPN)

### 7. BINDING OF PEANUT LECTIN TO GERMINAL-CENTRE CELLS: A MARKER FOR B-CELL SUBSETS OF FOLLICULAR LYMPHOMA?

**Rose ML, Habeshaw JA, Kennedy R, Sloane J, Wiltshaw E, Davies AJ**
**Chester Beatty Res. Inst., Fulham Road, London SW3 6JB, England**
**Br J Cancer; 44(1):68-74 1981**

The binding of horseradish-peroxidase-labeled peanut lectin (HRP-PNL) to cryostat sections of tonsil, lymphoma lymph nodes, reactive lymph nodes and miscellaneous tumors demonstrated that PNL binds selectively to lymphocytes in germinal centers. Lymph nodes from 21 patients with non-Hodgkin's lymphomas were phenotyped as cell suspensions for PNL binding, and the following surface markers: E rosetting, C3d, SIg, OK markers of T-cell subsets, Ig heavy-chain and light-chain classes. There was a positive correlation between PNL binding and cells with SIg and C3d receptors. 4/5 cases of centroblastic/centrocytic follicular lymphoma had a PNL+ SIg+ C3d+ phenotype. Both cases of centroblastic/centrocytic diffuse lymphoma were PNL-. There was no correlation between PNL binding and heavy- or light-chain Ig class. PNL binding and presence of C3d receptors were not always positively correlated, indicating that follicular cells may be either PNL+ SIg+ C3d+ or PNL+ SIg+ C3d-. The binding pattern of PNL to one case of thymic hyperplasia and two cases of malignant lymphoma lymphoblastic T type suggested that some but not all cortical thymocytes bind PNL. (Author abstract) (9 Refs)

### 8. THE SELECTIVE USE OF CYTOCHEMISTRY AND SURFACE MARKERS FOR THE DIAGNOSIS OF LEUKEMIAS AND LYMPHOMAS--A PRACTICAL APPROACH.

**Sun T**
**Dept. Pathology, Cornell Univ. Medical Coll., New York, NY**
**Lab Med; 12(7):424-431 1981**

Most leukemias and lymphomas can be identified by a few cytochemical tests: myeloperoxidase (positive in myeloid leukemias), chloroacetate esterase (specific esterase; positive in myelocytes), alpha-naphthyl butyrate esterase (nonspecific esterase; diffusely positive in monocytes, focally positive in T-lymphocytes), E-rosetting (T-cells), and several immunoglobulin (Ig) antisera. Other tests include PAS staining, assays for acid phosphatase, terminal deoxynucleotidyl transferase (TdT), leukocyte alkaline phosphatase, lysozyme, cytoplasmic Ig, Fc and complement receptors, and binding to mouse RBC (MRBC) the total B-cell count and the ratio of different classes of surface light and heavy chains distinguishes between benign and malignant lymphoproliferative diseases. The presence of a monoclonal surface Ig on 75% or more of the B-cells indicates a malignant lymphoma. If the surface Ig is polyclonal, a neoplasm cannot be definitely excluded but a benign condition is more probable. A markedly elevated number of phagocytic cells suggests a monocytic or histiocytic neoplasm. Other markers associated with malignancy include selective depletion of normal markers, the coexistence of multiple markers that normally are not present in combination (eg, T-cell and B-cell markers on the same cells), markers for immature cells (cytoplasmic Ig in non-plasma cells, also TdT), and rosette formation with MRBC. The use of polyvalent Ig antisera and monospecific antisera against IgG, IgM, IgA, IgD, and the kappa and lambda chains is sufficient to identify most lymphomas and lymphoid leukemias. (28 Refs)

### 9. AN ENZYME- AND IMMUNOHISTOCHEMICAL STUDY OF MALIGNANT LYMPHOMAS.

**Hachiya T, Watanabe S, Shimoyama M, Minato K**
**(c/o Watanabe) Second Section Pathology Div., Natl. Cancer Center Res. Inst., 1-1, Tsukiji 5-chome, Chuo-ku, Tokyo 104, Japan**
**Jpn J Clin Oncol; 11(1):93-100 1981**

Thirty-three consecutively biopsied specimens of malignant lymphomas (including 18 B-cell, 11 T-cell, and 1 non-T-non-B) were studied enzyme-histochemically in relation to histologic typing, immunologic markers and tissue intracellular immunoglobulin (cIg). Three cases of Hodgkin's lymphoma and two of infectious mononucleosis were also examined. All seven follicular lymphomas showed B-cell characters and 11/18 diffuse lymphomas were B-cell lymphomas, six were T-cell and one was non-T-non-B. Of the 11 T-cell lymphomas, five were immunoblastic lymphadenopathy-like T-cell lymphomas. Cell suspensions from the lymph nodes of the patients with Hodgkin's lymphomas and infectious mononucleosis did not reveal any immunologic monoclonality. Alkaline phosphatase activity was found in only one follicular lymphoma in which ATP-ase activity was also observed. ATP-ase activity was detected in six B-cell and two T-cell lymphomas. Acid phosphatase was found in three T-cell and two B-cell lymphomas. Significant beta-glucuronidase and esterase activities were not present in neoplastic cells, except for three cases which were weakly positive for beta-glucuronidase. Alpha-N-butylate esterase and N-chloroacetate esterase were not demonstrated. cIg was positive in 7/15 B-cell lymphomas. Five of them had mu and kappa chains, one showed gamma and lambda chains, and the other one had only a lambda chain. Monoclonality of cIg was in accordance with surface immunoglobulin of neoplastic cells. None of the 11 T-cell lymphomas revealed cIg. The results indicated that the enzyme activities are not sufficient to determine the T- or B-cell character of these neoplasms. (31 Refs)

### 10. CELL TYPING IN LYMPHOPROLIFERATIVE DISORDERS: USE OF A SENSITIVE HEMADSORPTION TECHNIQUE FOR SECTIONS OF NORMAL AND ABNORMAL LYMPHOID TISSUE.

**Wood WG, Hood P, Rippey JH**
**Dept. Pathology, St. Luke's Hosp., Wornall Road at 44th, Kansas City, MO, 64111**
**Am J Surg Pathol; 5(4):369-379 1981**

A hemadsorption technic originally devised to detect constant fragment (Fc) receptors on human cancer was applied to normal, reactive, and neoplastic human lymphoid tissue. The specimens studied were biopsies from patients with non-Hodgkin's lymphoma (NHL: 74), nodular sclerosis and mixed cellularity Hodgkin's disease (HD: 16), and immunoblastic lymphadenopathy (IBL: 4). The wells of microculture slides were

filled with sheep RBC variously sensitized with IgM and complement (EAC soln for detecting complement receptors on B-cells and some but not all M-cells), IgG only (EA soln for detecting Fc receptors on M-cells), IgM only (MEA soln to control for nonspecific adherence, and with unsensitized sheep cells (E soln for detecting T-cells). The patterns observed in normal tonsil, thymus, spleen, and lymph node tissue are described. The neoplastic nodules in 30/32 nodular NHLs showed crisp binding of only EAC soln, indicating a B-cell origin. A majority of 42 diffuse NHL lymphomas were also marked as B-cell lesions. No markers could be demonstrated in six diffuse lymphomas which were relegated to the U-cell category. The 16 HD lymph node specimens all showed approx equal adherence of EAC, EA, and E soln. Six of the 16 nodes contained MEA-positive cells. Specimens from IBL patients avidly adsorbed EAC soln only, suggesting that the proliferating cells were derived from B-lymphocytes. The simplicity and accuracy of this technic for categorization of different cells in normal lymphoid organs and in certain lymphoproliferative disorders are discussed. (49 Refs)

### 11. BURKITT'S TYPE ACUTE LYMPHOBLASTIC LEUKEMIA. CELLULAR PHENOTYPE AND CHROMOSOME ABNORMALITIES.

Demeocq F, Bernard A, Boumsell L, Bezou MJ, Turchini MF, Malpuech G
Laboratoire d'Hematologie, Clinique Medicale Infantile, Hotel-Dieu, BP69, 69003 Clermont-Ferrand, France
Arch Fr Pediatr; 38(5):355-357 1981

The immunologic and cytogenetic analysis of a 13-yr old male patient with Burkitt's type acute lymphoblastic lymphoma is described. The lymphoblasts were found to carry IgS mu and gamma, with no IgD, and with only weak expression of the receptors for the constant fragment of IgG. This phenotype corresponded with a highly differentiated B cell line. A translocation between chromosomes 1 and 8 was observed. The implications of these findings are discussed. (12 Refs) (In FRE)

### 12. SPONTANEOUS AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY BY LYMPHOCYTE SUBPOPULATIONS IN PERIPHERAL BLOOD AND SPLEEN FROM ADULT UNTREATED PATIENTS WITH HODGKIN'S DISEASE.

Gupta S, Fernandes G
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Clin Exp Immunol; 45(1):205-214 1981

Subpopulations of lymphocytes in the peripheral blood and spleen from adult untreated patients with Hodgkin's disease were studied for spontaneous (SCMC) and antibody-dependent cellular cytotoxicities (ADCC). Peripheral blood from 7 of 24 patients demonstrated abnormally low T cell-mediated SCMC when compared to age- and sex-matched healthy controls. Only two of these patients also demonstrated low T cell ADCC and non-T cell-mediated SCMC and ADCC. T cell ADCC in the peripheral blood of patients with involved spleen was significantly higher (p less than 0.05) when compared to those in whom spleen was not involved. When SCMC and ADCC were compared between peripheral blood and splenic lymphocytes with regard to involvement of spleen by Hodgkin's disease, non-T cell SCMC in the involved spleen was significantly lower (p less than 0.05) than their peripheral blood non-T cell SCMC. SCMC and ADCC tended to be higher in patients with Stages III and IV of Hodgkin's disease when compared to those with Stages I and II. However, the differences were not statistically significant. No direct relationship was observed between T cell SC MC or ADCC and the proportion of T cells with IgG Fc receptors (Tgamma). The significance of these observations is discussed. (Author abstract) (56 Refs)

## DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS

### 13. A NOVEL LYMPHOCYTE FUNCTION-ASSOCIATED ANTIGEN (LFA-1: CELLULAR DISTRIBUTION, QUANTITATIVE EXPRESSION, AND STRUCTURE.

Kurzinger K, Reynolds T, Germain RN, Davignon D, Martz E, Springer TA
Lab. Membrane Immunochemistry, Sidney Farber Cancer Inst., Harvard Medical Sch., Boston, MA, 02115
J Immunol; 127(2):596-602 1981

We have previously described a monoclonal antibody (MAb), M7/14, which blocks a variety of T cell functions, including CTL-mediated killing, the mixed lymphocyte response, and antigen-specific proliferation. The antigen defined by M7/14 has been designated lymphocyte function-associated antigen one (LFA-1). In this report, LFA-1 has been studied as to cell distribution, surface abundance, structure, and in comparison to other CTL surface antigens. LFA-1 is expressed on lymphoid cells of both the T and the B lineages and on a large fraction of bone marrow cells, but not on exudate macrophages or nonlymphoid tissues. T cells express more LFA-1 than B cells, both in the unstimulated and stimulated states. Compared with unstimulated spleen cells, cytolytic T lymphocyte cell preparations (CTLP) and Con A blasts, but not LPS blasts, show increased LFA-1 expression relative to H-2, and for T cell-containing populations, Lyt-2. M7/14 MAb binds to about 1.5 x 10(4) LFA-1 sites per av spleen cell or CTLP cell, respectively. M7/14 MAb binds to CTLP in quantities of 2.5-fold and is 10.4-fold less than H-2 and Thy-1 MAb, respectively; since the latter have little or no effect on CTL function, inhibition of killing by M7/14 MAb is specific for the LFA-1 surface site. M7/14 MAb and a blocking Lyt-2 MAb are bound in similar quantities of CTLP. LFA-1 is a glycoprotein and consists of 2 noncovalently linked polypeptide chains of 180,000 and 95,000 Mr. The same molecular species as on CTL is present on other T cells and on B cells. The molecular structure and cell distribution of LFA-1 clearly distinguishes it from Lyt-2,3, Ly-5, T145, and T11, which were previously suggested to be either associated with the function of and/or present on the surface of CTL. (Author abstract) (42 Refs)

### 14. UBIQUITOUS CELL-SURFACE GLYCOPROTEIN ON TUMOR CELLS IS PROLIFERATION-ASSOCIATED RECEPTOR FOR TRANSFERRIN.

Sutherland R, Delia D, Schneider C, Newman R, Kemshead J, Greaves M
Membrane Immunology Lab., Imperial Cancer Research Fund, Lincoln's Inn Fields, London WC2A 3PX, England
Proc Natl Acad Sci USA; 78(7,part2):4515-4519 1981

A murine monoclonal antibody (OKT9) raised against human leukemic cells binds to a wide variety of leukemia and tumor cell lines and to a minority of leukemia cells taken directly from pat ients. Fetal thymus and liver are strongly reactive as are some normal, immature hemopoietic cells and acti-

vated lymphocytes. Reactivity with OKT9 appears to correlate with proliferation status in both normal and malignant populations. Biochemical analysis indicates that this structure is a approx 180,000-dalton glycoprotein with two disulfide-bonded subunits of approx 90,000-daltons. Isolation of the transferrin receptor from a T-cell line (MOLT-4) indicates that it also has a dimeric approx 180,000-dalton structure. Radio-labeled transferrin bound to its receptors can be specifically precipitated by the monoclonal OKT9, although the latter does not bind transferrin itself, indicating that the antigenic structure defined by this antibody is likely to be the transferrin receptor. (Author abstract) (37 Refs)

### 15. TUMOUR MARKERS: THEIR ROLE IN CLINICAL MEDICINE.

**Dearnaley DP, Coombes RC**
**Clinical Oncology Unit, Ledwig Inst. Cancer Res. (London Branch), Royal Marsden Hosp., Sutton, Surrey, England**
**Practitioner; 225(1356):839-841,843-844,846-849 1981**

Biochemical tumor markers currently used in diagnosis and monitoring responses to treatment are human chorionic gonadotropin (HCG) in trophoblastic tumors; beta subunit HCG and alpha-fetoprotein (AFP) in testicular tumors; AFP (if the initial titer is very high) in hepatomas; acid phosphatase in prostatic cancer; catecholamines in neuroectodermal tumors; and calcitonin in medullary carcinoma of the thyroid. Carcinoembryonic antigen (CEA) assays are useful for monitoring responses to treatment in patients with colorectal cancer, but cannot be used in diagnosis. Certain lung tumors (especially oat cell carcinomas) secrete ectopic ACTH, antidiuretic hormone, and/or calcitonin. These ectopic hormones may also be present in patients with chronic obstructive pulmonary disease, but the ectopic hormones associated with lung cancer are often of abnormally high mol wt. Assays for these high-mol wt hormones may be useful for monitoring responses to therapy. Adenocarcinomas and squamous cell carcinomas of the lung may produce CEA, alkaline phosphatase, and gamma-glutamyl transpeptidase. However, elevated CEA levels are present in smokers and patients with many non-neoplastic and inflammatory diseases, and the enzymes are not tumor-specific. At present, the role of biochemical markers in the management of the common solid tumors is rather limited. The use of tumor markers in breast and lung cancer must await further research. Monoclonal antibody technology should soon provide satisfactory antibodies for immunolocalization and immunocytochemistry studies in breast cancer patients. (12 Refs)

### 16. MULTIPLE MYELOMA ASSOCIATED IDIOTYPE BEARING LYMPHOCYTES: CHARACTERIZATION OF THE CELL TYPE AND THE ACQUISITION OF AN ENRICHED POPULATION.

**Smith LJ**
**State University of New York, Buffalo, NY**
**Diss Abstr Int (B); 42(1):148-B 1981**

In our studies of eight IgG myeloma patients, we have found that 0-40% of their peripheral blood mononuclear cells exhibited patient specific idiotypic markers. We have extended previous work by subtyping this cell population and by isolating it. Immunofluorescent techniques were used to recognize in various combinations surface idiotypes, Fc(IgG) receptors, IgM-IgD determinants and peroxidase positivity. Rosetting techniques were used with Ficoll Hypaque centrifugation to fractionate cells into rosetting and nonrosetting populations. A subpopulation of Fc(IgG) receptor bearing lymphocytes that did not bind sheep RBC was purified by removing the EAET rosetting cells, followed by removal of nylon wool adherent cells. The idiotype bearing cells could be pelleted along with EA but not with EAET or EAC rosetting reagents. After the latter two procedures, cells exhibiting myeloma associated idiotypes were retained at the Ficoll Hypaque interface in enriched numbers. The cell subpopulation obtained by the two step purification method consisted of 90-99% Fc(IgG) receptor bearing lymphocytes of which 17-99% also exhibited the myeloma associated surface idiotype. Cells with these idiotypic markers thus resembled normal donor peripheral blood lymphocytes that have Fc(IgG) receptors, but lack receptors for sheep RBC. (no Refs)

### 17. FC RECEPTOR-BEARING PERIPHERAL BLOOD MONONUCLEAR CELLS IN BREAST CANCER PATIENTS: A POSSIBLE MARKER OF TUMOUR BURDEN AND PROGNOSIS.

**Bray J, McPherson TA**
**Cross Cancer Inst., 11560 University Ave., Edmonton, Alberta T6G 1Z2, Canada**
**Clin Exp Immunol; 44(3):629-637 1981**

Indirect immunofluorescence was used to identify and quantitate peripheral blood mononuclear (PBM) cells possessing high avidity Fc receptors in 105 patients upon referral to the breast cancer clinic at the Cross Cancer Institute. The cell detected was shown to be a non-adherent PBM, probably belonging to the T or null cell population. The mean percentage +-2 standard deviations of PBM-positive cells in 75 patients with no disease or benign breast disease was 5.3 +-6.7, and this was significantly (p less than 0.001) less than the percentage found for 31 patients with breast cancer. The percentage of PBM-positive cells correlated directly with tumor burden in patients with small (less than or equal to 5 cm) tumors without regional node or extranodal metastases (5/13 had greater than or equal to 12% positive PBM) and in those with small tumors plus regional node metastases, but without extranodal metastases (8/10 had greater than or equal to 12% positive PBM). This correlation was less, however, in patients with large tumors (greater than 5 cm), and in those with extranodal metastases (4/8 had greater than or equal to 12% positive PBM), and in patients tested postoperatively (1/13 had greater than or equal to 12% positive PBM) even though 6/13 had regional node metastases at the time of surgery. Thus, this relatively simple assay, which can be done on peripheral blood samples, may turn out to be useful in patients with breast cancer as a prognostic marker insofar as it may be an indirect indicator of tumor burden preoperatively. If so, it may lead to a more aggressive postoperative adjuvant therapy approach to the subpopulation of node-negative PBM-positive breast cancer patients than is currently used for node-negative patients. (Author abstract) (26 Refs)

### 18. DECISIVE PROGRESS IN MARKER STUDIES OF NORMAL AND MALIGNANT CELLS: MONOCLONAL ANTIBODIES AND FLOW MICROFLUOROMETRY.

**Bernard A, Boumsell L, Bayle C, Raynal B, Pham D, Coppin H, Richard Y**
**Laboratoire d'Immunologie des Tumeurs de l'Enfant, Insitut Gustave-Roussy, 94800 Villejuif, France**
**Arch Fr Pediatr; 38(5):369-374 1981**

Biological markers indicative of various lymphocyte pathologies, particularly their neoplastic transformation (lymphomas and leukemias) are discussed. The role of serological analysis in the study of cell surface markers is described along with a dis-

cussion of the difficulties encountered with classic serological analysis. Lymphocyte hybridization and the development of monoclonal antibodies are described along with the detection of the binding of antibodies on cell surface antigens by flow microfluorometry. The determination of the levels of T lymphocyte differentiation and the identification of T cell subpopulations through the use monoclonal antibodies is described. The possibility of using monoclonal antibodies to define the tumor surface antigens in man is discussed. The antigenicity of non-T, non-B acute lymphoblastic leukemia and the therapeutic implications of this form of leukemia are discussed. (26 Refs) (In FRE)

## 19. BREAST EPITHELIAL CELL SURFACE COMPONENTS CHARACTERIZED BY MONOCLONAL ANTIBODIES (MEETING ABSTRACT).

**Peterson JA, Ceriani RL**
**Bruce Lyon Memorial Research Laboratory, Children's Hospital Medical Center, Oakland, CA, 94609**
**4th Annual San Antonio Breast Cancer Symposium, Nov 6-7, 1981, San Antonio, Texas Cancer Therapy and Research Center of South Texas; 1981**

Monoclonal antibodies were prepared to components of the cell surface of breast epithelial cells using human milk fat globule membranes (HMFGM) as a source of antigens. Spleen cells from BALB/c mice, immunized with HMFGM, were fused with either producing or non-producing mouse myeloma cells. The resulting hybridomas were screened by a solid phase radioimmunoassay against membranes of normal breast epithelial cells and a battery of non-breast cells, and only those with a high or complete specificity for breast epithelial cells were retained. With a solid phase methodology it was possible to determine mol wt, and so far several monoclonal antibodies have been prepared that detect cell surface components with apparent mol wt of 45,000 and 400,000 respectively. The later component was a glycoprotein with a very high sugar content. Further, quantitative levels of these antigens in normal and neoplastic breast epithelial cells were obtained by a competitive radioimmunoassay. Both by radioimmunoassay and by indirect immunofluorescence it was established that human breast tumors are composed of heterogeneous cell populations where the antigens detected by our battery of monoclonals vary quantitatively from cell to cell, and are sometimes even deleted. However, each cell line or breast tumor has a fixed pattern of expression of these antigens. This variability of breast tumor cells contrasts with rigid expression of normalcy found in normal breast tissue. (no Refs)

## 20. MEMBRANE IMMUNOGLOBULINS OF SPONTANEOUS B LYMPHOMAS OF AGED BALB/C MICE.

**Laskov R, Kim JK, Woods VL, McKeever PE, Asofsky R**
**The Hubert H. Humphrey Centre for Experimental Medicine and Cancer Res., The Hebrew Univ.-Hadassah Medical Sch., Jerusalem, Israel**
**Eur J Immunol; 11(6):462-468 1981**

Four cell lines derived from spontaneous BALB/c B lymphoma tumors were analyzed with regard to the type of their membrane immunoglobulins (Ig). Using lactoperoxidase iodination of membrane proteins combined with immunoprecipitation and electrophoresis on polyacrylamide gel, three of these cell lines (X16c, L10A and K46) were found to express the monomeric form of IgM and IgD as well as half molecules. One cell line (M12) lacked both IgM and IgD. The apparent mol wt of the lymphoma mu chain was about 80,000 and exceeded the mol wt of 75,000 determined for mu chains secreted by myeloma cells. The mol wt of the delta heavy chain was found to be 66,000. Immunofluorescence showed that the L10A and X16c lines expressed lambda light chains on their cell surface. Another Ig-bearing cell line (K46) expressed both lambda and chi chains. Thus, three out of the four B lymphomas examined expressed both IgM and IgD with light chains of the lambda type. These results, together with our previous findings which demonstrate the presence of Ia and Fc receptors on the same cells, indicate that spontaneous B lymphomas in BALB/c mice are the malignant counterpart of mature B lymphocytes. (Author abstract) (39 Refs)

## 21. PLASMA MEMBRANE ENZYMES IN BALB/C LYMPHOMAS WITH EITHER T OR B CELL PROPERTIES. I. 5'-NUCLEOTIDASE.

**Zachowski A, Simonin G, Aubry J, Pommier P, Singh SN, Potter M, Paraf A**
**ERA 802 CNRS, Laboratoire d'Immunologie Cellulaire EPHE, Station de Recherches de Virologie et d'Immunologie, INRA, 78850 Thiverval-Grignon, France**
**J Receptor Res; 2(1):97-118 1981**

Membrane-bound 5'-nucleotidase activity was compared in crude extracts and plasma membrane fractions from murine plasmacytomas and thymomas. Clones of the tumor cells, judged representative of different steps in B and T cell differentiation according to surface antigen markers, were derived, respectively, from Abelson virus transformed lymphomas and IgM, IgA, and IgG producing plasmacytomas, and from thymomas with surface antigen markers characteristic of T suppressor and helper cells and of early T cell differentiation. Membrane fractions were obtained through cell lysis and purification. 5'-Nucleotidase activity was characterized by the following criteria: 1) optimal pH for enzyme activity (7.5-9.5 for B type lymphocytes and 5.5-6.5 for T type cells, except in Lut 13 membranes where it was 9.5); 2) specificity of 5'-AMP as a substrate at optimal pH (for all B cell categories and Lut 13, 5'-AMP was the best substrate; for the remaining T cell types pNPP was preferred); 3) specific inhibition of 5'-nucleotidase by alpha-beta methylene ADP at optimal pH (B type cells exhibited 50% inhibition between 10 and 300 uM, whereas T type membranes required greater than 1 milliM); and 4) inhibition by EDTA at pH optimum (for B derived and Lut 13 membranes, inhibition of 5'-AMP hydrolysis occurred between 0.1 and 5 milliM EDTA, but in T type cells no inhibition was seen). 5'-Nucleotidase was found to be present on Abelson virus transformed lymphomas, plasmacytomas, and LPS stimulated blasts from nu/nu spleen, but on no thymomas except Lut 13. 5'-Nucleotidase could be a key enzyme in the purine metabolism of B cells, but not in T cells. (50 Refs)

## 22. LOCALIZATION OF THE ABELSON MURINE LEUKEMIA VIRUS PROTEIN IN A DETERGENT INSOLUBLE MATRIX: ARCHITECTURE OF THE PROTEIN (MEETING ABSTRACT).

**Boss MA, Dreyfuss G, Baltimore D**
**Department of Biology, Center for Cancer Research, Massachusetts Institute of Technology, Cambridge, MA, 02391**
**RNA Tumor Viruses, May 20-24, 1981, Cold Spring Harbor, New York. Cold Spring Harbor Laboratory 294 pp., 1981.**

Abelson murine leukemia virus (A-MuLV) encodes a 120,000 mol wt protein called P120. P120 is a phosphorylated surface membrane protein, which when incubated with 32P-ATP following immunoprecipitation becomes labeled with 32P on tyrosine residues. We have studied the interaction of P120 with other cellular components following extraction with the

non-ionic detergents Triton X-100. Most of the A-MuLV P120 associated kinase activity was found with the detergent insoluble matrix (DIM) of both lymphoid and fibroblast cell lines. However, studies of the distribution of the 35S-methionine and 32PO(4)-labeled protein revealed a more complex pattern. P120 labeled during a short period of exposure of cells to 35S-methionine was mainly in the DIM (lymphoid cells) or equally distributed in the DIM and the soluble fractions (fibroblasts). Steady state labeled P120 was distributed equally in the two fractions (lymphoid cells) or mostly in the soluble portion (fibroblasts). Thus there was an apparent movement of P120 from the DIM to the detergent soluble fraction. When the DIM was incubated with 32P-ATP in situ, phosphorylation of tyrosine residues of P120 was observed. An 80,000 mol wt fragment of P120 (F80) was found after extraction of fibroblastic cells with detergent. F80 was not found in extracted lymphoid cells but mixing labeled lymphoid cells and unlabeled fibroblasts before extraction produced the fragment. F80 contained the gag determinants of p120 but did not react with Abelson-specific serum. (no Refs)

## 23. IDENTIFICATION OF AN ABELSON MURINE LEUKEMIA VIRUS-ENCODED PROTEIN RELATED TO P120 ON THE PLASMA MEMBRANE OF TRANSFORMED LYMPHOID CELLS (MEETING ABSTRACT).

**Machida C, Kabat D**
**Departments of Microbiology and Immunology, University of Oregon Health Sciences Center, Portland, OR**
**RNA Tumor Viruses, May 20-24, 1981, Cold Spring Harbor, New York. Cold Spring Harbor Laboratory 294 pp., 1981.**

A lymphoid cell line (L1-2) transformed by Abelson murine leukemia virus (A-MuLV) contains two virus-encoded proteins - p120 plus a small amount of a structurally related protein with an apparent Mr of 95,000 (p95). A novel surface detection technique suggests that p95, but not p120, occurs on the outer surface of cellular plasma membranes. This molecule is both immunologically and structurally related to A-MuLV p120, containing the gag related regions, p15 and p12, and limited portions of the unique 'x' host-encoded region. The p95 molecule is detected on the surface of this A-MuLV transformed lymphoid cell line only with tumor regressor serum recognizing this unique 'x' determinant. Tryptic peptide analysis of [35S] methionine-labeled proteins shows that p95 contains at least 7 peptides found in p120. Immunoprecipitated p95 can become phosphorylated in vitro by incubation with [gamma-32P] ATP and has been shown to contain the tyrosine-containing phosphorylation site previously described for p120. These results suggest that p120 may occur at intracellular site(s) in A-MuLV transformed cells. (no Refs)

## 24. A NEW MOUSE CELL-SURFACE ANTIGEN (LY-M18) DEFINED BY A MONOCLONAL ANTIBODY.

**Kimura S, Tada N, Liu Y, Hammerling U**
**Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021**
**Immunogenetics; 13(6):547-554 1981**

Spleen cells from C3H/An mice immunized with spleen cells of C57BL/6-H-2k mice were fused with myeloma cell line NS.1. One established hybrid cell line continuously secreted antibody that recognized a new surface antigen provisionally called Ly-m18. The new alloantigen is expressed on 90% of thymus cells, 55% of spleen cells, and 45% of either lymph-node or bone-marrow cells. It is also expressed on cells derived from brain, kidney, and liver. Fifty percent of either peripheral T or B cells express the Ly-m18 antigen, and some tumor cell lines with T, B, pre-B or stem cell characteristics are Ly-m18 (+). The strain distribution pattern distinguishes Ly-m18 antigen from all other murine lymphocyte alloantigens. The typing data of two sets of CXB and AKXL recombinant inbred strains indicate that the Ly-m18 gene is linked to the Ltw-2 locus which has not yet been assigned to a chromosome. (Author abstract) (30 Refs)

## 25. LYMPHOCYTE FUNCTION-ASSOCIATED ANTIGEN 1 (LFA-1): A SURFACE ANTIGEN DISTINCT FROM LYT-2,3 THAT PARTICIPATES IN T LYMPHOCYTE-MEDIATED KILLING.

**Davignon D, Martz E, Reynolds T, Kurzinger K, Springer TA**
**(c/o Springer), Sidney Farber Inst., Harvard Medical Sch., Boston, MA, 02115**
**Proc Natl Acad Sci USA; 78(7,part2):4535-4539 1981**

Monoclonal antibodies (MAb) have been used to probe the relationship of cytolytic T lymphocyte (CTL) surface molecules to CTL function. Rat MAb to mouse CTL were generated. Twelve MAb so obtained gave preferential binding to T cells as compared to B cells, and three of these recognized previously undescribed surface polypeptides. These MAb and more broadly reactive and previously obtained MAb were tested for their ability to block CTL-mediated killing in the absence of complement. To ensure that any observed blocking was due to binding of MAb to the effector cell rather than the target cell, a xenogeneic mouse CTL anti-rat BN lymphoma target cell system was utilized (MAb and target cells both of rat origin). Of 24 MAb tested here, 21 had little or no effect on CTL function, including those to H-2, Thy-1, Lyt-1, Ly 5, Ly 6, Lgp 100, and at least six other defined antigens. We confirmed inhibition of killing with two MAb to Lyt-2,3. Another MAb, M7/14, gave profound and consistent blockade of CTL function. It was confirmed that M7/14 MAb blocks killing by binding to the mouse CTL and does not bind to the rat lymphoma target cells used for the CTL assay. The findings suggest that the antigen defined by M7/14, termed a lymphocyte function-associated antigen, LFA-1, participates in or is closely associated with the mechanism of CTL-mediated killing. LFA-1 contains two polypeptide chains of 180,000 and 95,000 Mr and is distinct from other described lymphocyte glycoproteins. LFA-1 thus represents both a previously undescribed lymphocyte surface antigen and molecular site for blockade of CTL-mediated killing. (Author abstract) (49 Refs)

## 26. THE G-IX ANTIGEN OF MURINE LEUKEMIA VIRUS: AN ANALYSIS WITH MONOCLONAL ANTIBODIES.

**Pierotti M, DeLeo AB, Pinter A, O'Donnell PV, Hammerling U, Fleissner E**
**Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY**
**Virology; 112(2):450-460 1981**

The GIX antigen of murine retrovirus gp70 is a marker for virus replication in various cell types, as well as for T-cell differentiation and leukemogenesis in particular mouse strains. The serological definition of GIX depends on the cytotoxicity of a particular rat antiserum for thymocytes from strain 129 mice. We have found that two rat monoclonal antibodies, elicited by immunization with AKR ecotropic virus or AKR leukemia cells, co-type closely with GIX in several assay systems. Like GIX, the epitopes identified by the monoclonal antibodies are amplified on thymocytes during leukemogenisis in AKR mice. These antibodies are cytotoxic for GIX+ leukemia cells and for fibroblasts infected with GIX+ viral serotypes.

Though absorbed by GIX+ thymocytes of various strains, the antibodies are not cytotoxic for these cells. We ascribe the latter result to lower representation of antigenic sites on normal thymocytes, and postulate that more than one epitope may participate in classical GIX-mediated cytotoxicity. The monoclonal antibodies do not react with viral env products synthesized in the presence of the inhibitor of glycosylation, tunicamycin. Reactivity with the antibodies appears to require a stable configurational change in the env precursor protein coinciding with glycosylation, rather than direct participation of carbohydrate in the antigenic site. Thus subsequent enzymatic removal of carbohydrate chains in vitro does not alter reactivity with the antibodies. (Author abstract) (42 Refs)

### 27. FELINE LEUKEMIA - UNIQUE AND CROSS-REACTING ANTIGENS ON INDIVIDUAL VIRUS-PRODUCING TUMORS IDENTIFIED BY COMPLEMENT-DEPENDENT ANTIBODY.

**Grant CK, Michalek MT**
**Dept. Microbiology, Harvard Sch. Public Health, 677 Huntington Ave., Boston, MA, 02115**
**Int J Cancer; 28(2):209-217 1981**

Following exposure to feline leukemia virus (FeLV), cats that resist leukemia produce complement dependent antibodies (CDA) which lyse leukemia cells in the presence of cat complement. The CDA activity has been shown to be directed to feline oncornavirus-associated cell membrane antigen (FOCMA) found on the surface of most feline leukemias. Despite the retrovirus etiology of feline leukemia, and the ubiquity of FOCMA expression by individual tumors, we found that CDA activity did not cross-react when five feline leukemia lines were compared (FL74, F422, 3272, 3281, and 79-14940). Profiles for CDA mediated lysis of the leukemia target lines were determined for sera from 149 FeLV exposed cats, and animals were identified whose sera would selectively lyse almost any possible combination of tumors from one to five lines tested. Cross absorption and cold target inhibition studies were performed on selected sera, and a spectrum of different antigens was identified which included both individual determinants and antigens shared by some of the tumor lines. Leukemias FL74 and F422 carried a cross-reactive determinant which was distinct from a second antigen shared by 3272 and 3281; lines F422, 3272 and 3281 each also carried a unique antigen. Leukemia 79-14940 did not cross-react with other target tumor lines. Targets of CDA mediated lysis on leukemia cells may be associated with normal feline cell surface antigens, because CDA titers were sometimes reduced after serum absorption with normal cat spleen cells. The relevance of multiple FOCMA determinants is discussed in terms of tumor escape from immunity. (Author abstract) (30 Refs)

### 28. FELINE ONCORNAVIRUS-ASSOCIATED CELL MEMBRANE ANTIGEN (FOCMA) EXPRESSION: CURRENT CONCEPTS FROM IMMUNOFLUORESCENCE AND IMMUNOPRECIPITATION DATA USING MONOCLONAL ANTIBODIES (MEETING ABSTRACT).

**VedBrat SS, Prensky W, Lutz H, Ruscetti S**
**Sloan-Kettering Institute for Cancer Research, New York, NY**
**RNA Tumor Viruses, May 20-24, 1981, Cold Spring Harbor, New York. Cold Spring Harbor Laboratory 294 pp., 1981.**

We investigated the binding properties of a series of monoclonal antibodies (MAs) to putative FOCMA-L determinants with antigens expressed in (a), a group of standard cells characterized by parallel assays with standard antisera to FOCMA and structural antigens of feline leukemia virus (FeLV), and (b), in cat or mink cells experimentally infected with virus obtained from the standard cells. We found that: (1), eleven of 18 antibodies also react with non-transformed cells infected by FeLV-C, but not with cells infected by FeLV-A. (2) Some of the MAs reacted with both FOCMA-L and FOCMA-S. (3) F422 cells, which lack infectious FeLV-C or FeLV-B, express antigen with epitopes common to FeLV-C and FOCMA-L. The reported absence of FOCMA determinants from viral proteins is not true for FeLV-C. In our hands cat antisera to FOCMA do not readily distinguish FOCMA from FeLV-C. Many of the reported FOCMA-positive and FeLV-negative cat lymphomas may well have been positive for FeLV-C. Our evidence is consistent with a model which predicts that the genetic material coding for FOCMA-L and FeLV-C arise as recombinant sequences in FeLV-A infected cats, and the FeSV can arise as a result of a second recombination event between such sequences and a feline cellular sarc gene. The latter is supported by the observation that transforming virus can be obtained by the in vitro infection of cat fibroblasts with FeLV-C, but not by their infection with FeLV-A. (no Refs)

## LYMPHOCYTE AND DIFFERENTIATION ANTIGENS

### 29. T LYMPHOCYTES SPECIFIC FOR IMMUNOGLOBULIN ALLOTYPE. I. IGH-1B-SPECIFIC T CELLS DEMONSTRATED BY SUPPRESSION IN VIVO AND CYTOTOXICITY IN VITRO.

**Snodgrass HR, Wilson DB, Bosma MJ**
**Div. Res. Immunology, Dept. Pathology, Univ. Pennsylvania Sch. Medicine, Philadelphia, PA, 19104**
**J Exp Med; 154(2):480-490 1981**

The specificity of a population of thymus-derived suppressor lymphocytes (Ts) wa s determined using rosetting techniques. BALB/c mice were immunized with serum from C57BL/6 mice, which carried Igh-1b proteins. T cells from the immunized mice were rosetted with sheep RBC (SRBC) coated with Igh-1a or Igh-1b proteins, or with SRBC coupled with goat anti-mouse Ig (GAMIg). The T cells were then mixed with spleen cells from C.B.-17 mice, which carry the Ighb complex. Igh-1b production was suppressed in all mice receiveing T cells rosetted with Igh-1b. Only 20% of mice receiving non-Igh-1b were suppressed, indicating that the Ts were specific for the Igh-1b allotype. Spleen cells from Ighb-immune mice were restimulated in vitro with irradiated CB101, an Igh-1b-producing myeloma, and tested for cytolytic activity against labeled CB101 cells. The results showed that cytolytic activity required in vivo priming and in vitro restimulation. Non-Igh-1b-producing tumor cells did not restimulate cytolytic activity. Tests of cytolytic activity against several cell lines showed lysis only of Igh-1b cell lines. Purified Igh-1b proteins were shown to be capable of priming T cell response. Apparently the target in allotype suppression is a B cell. Allotype-specific cytotoxic T cells appear to be involved in the regulation of allotype expression in the suppressed state. (39 Refs)

## 30. T LYMPHOCYTES SPECIFIC FOR IMMUNOGLOBULIN ALLOTYPE. II. CLONED IGH-1B-SPECIFIC CYTOTOXIC T CELLS.

Snodgrass HR, Bosma MJ, Wilson DB

Div. Res. Immunology, Dept. Pathology, Univ. Pennsylvania Sch. Medicine, Philadelphia, PA, 19104

J Exp Med; 154(2):491-500 1981

Spleen cells from BALB/c mice immunized with Igh-1b myeloma proteins were restimulated three times. They were then cultured in the absence of antigen in medium supplemented with T cell growth factor (TCGF). The lytic activity of long-term cell lines was tested at various times against CB101 target cells. The cell lines and their clones were identified as T cells by their sensitivity to treatment with anti-Thy-1.2 and complement. Clones of T cells showed the same specificity for lysis of CB101 cells and nonlysis of CB101NP cells as the primary T cell populations. Clones were 30-100 times more potent than primary populations. The lytic capability of cloned T cells was inhibited by preincubation with Igh-1b. It was not inhibited by preincubation with Igh-1a, Igh-4a, or Igh-4b proteins. Igh-1b did not inhibit the activity of non-Igh-1b-specific T cells. A suggested mechanism for Igh-1b inhibition of T cell function is that Igh-1b serves to bridge two T cells, causing one to lyse the other. The results support a previous conclusion that allotype-bearing B cells are a target of T cells in allotype-suppressed mice. (13 Refs)

## 31. NATURAL KILLER CELLS KILL TUMOUR CELLS AT A GIVEN STAGE OF CELL DIFFERENTIATION.

Gidlund M, Orn A, Pattengale PK, Jansson M, Wigzell H, Nilsson K

Dept. Immunology, Univ. Uppsala Biomedical Center, Box 582, S-751 23 Uppsala, Sweden

Nature (Lond); 292(5826):848-850 1981

The effect of differentiation-inducing agents on the natural killer (NK)-cell susceptibility of three tumor cell lines was studied: K-562, a human erythroleukemia cell line; U-937, a human histiocytic lymphoma cell line; and GM-86, a murine Friend virus-induced leukemia originating in DBA/2J mice. The cells were tested for NK-sensitivity in a 57Cr-release assay, with Ficoll-Isopaque-isolated human peripheral blood cells used as effector cells for the human target cells and mouse spleen cells used as effector cells for the GM-86 target cells. The NK-cell sensitivity of K-562 cells decreased after exposure to sodium butyrate or hemin, and this decrease was correlated in time with an increase in erythroid differentiation markers. Treatment of U-937 cells with 12-O-tetradecanoylphorbol-13-acetate or supernatants from mixed lymphocyte cultures induced the appearance of cells with a macrophage-like appearance and resulted in a concomitant reduction in NK-cell sensitivity. Following hexametabisacetamide treatment, the GM-86 cells acquired the capacity of globin production but showed decreased NK-cell susceptibility. These results supported the hypothesis that susceptibility to NK cells may vary according to the differentiation stage of the tumor target cell. (24 Refs)

## 32. DISTRIBUTION OF SURFACE, CYTOPLASMIC AND SECRETED IGG SUBCLASSES IN HUMAN LYMPHOBLASTOID CELL LINES AND NORMAL PERIPHERAL BLOOD LYMPHOCYTES.

Simmons JG, Fuller CR, Buchanan PD, Yount WJ

Dept. Medicine, Div. Rheumatology and Immunology, Univ. North Carolina at Chapel Hill, 932 F.L.O.B. 231H, Chapel Hill, NC, 27514

Scand J Immunol; 14(1):1-13 1981

Twenty-two IgG-positive lymphoblastoid cell lines and normal peripheral blood lymphocytes were studied for surface and cytoplasmic IgG, IgG subclasses, IgD and IgM, using monospecific fluorescein- and rhodamine-conjugated F(ab')2 antibody fragments, and for secretion by double antibody radioimmunoassay. Several parallel observations and several differences in IgG subclass expression were noted between cell lines and normal lymphocytes. Surface IgG2 was frequently expressed in normal IgG-positive lymphocytes but was seldom expressed in cell lines. Cell lines resembled normal IgG-positive lymphocytes in the frequent expression of cytoplasmic IgG3 and IgG4, often without secretion. Cell lines and normal lymphocytes both showed more frequent distribution of IgG and IgG subclasses in cytoplasm than in surface immunoglobulin, and often a discrepancy of surface versus cytoplasmic IgG subclass. A good correlation was noted between surface, cytoplasmic and secreted IgG1. Despite a predominance of IgG2 and IgG4 surface IgG subclasses, and IgG3 and IgG1 in cytoplasm, secreted immunoglobulins from normal lymphocytes in short-ter m culture showed a similar distribution of IgG subclasses to that seen in normal sera. Multiple expression of IgG subclasses was much more frequent in IgG-positive cell lines than in normal peripheral blood lymphocytes, both in surface and cytoplasmic IgG. (Author abstract) (16 Refs)

## 33. SPECIFICITY OF FC RECEPTORS FOR IGG2A, IGG1/IGG2B, AND IGE ON RAT MACROPHAGES.

Boltz-Nitulescu G, Bazin H, Spiegelberg HL

Dept. Immunopathology, Res. Inst. of Scripps Clinic, La Jolla, CA, 92037

J Exp Med; 154(2):374-384 1981

Alveolar and peritoneal macrophages (M-phi) were obtained from Lewis and Brown Norway rats. The ability of M-phi to form rosettes with fixed ox RBC (Eo') coated with myeloma proteins of all Ig classes, and with fresh RBC (Eo) sensitized with rat IgG1 and IgG2, rabbit IgG and IgM, and mouse antibodies was measured. Rosettes were formed with Eo' coated with IgG1, IgG2a, IgG2b, and IgE myeloma proteins, but not with IgG2c, IgA, IgM, or IgD. Rosettes were also formed with Eo' coated with human IgG1, IgG3, IgG4, mouse IgG1, IgG2a, IgG2b, and rabbit IgG. Rosettes were formed with Eo sensitized with rat IgG1, IgG2, or rabbit IgG. No rosettes were formed with rabbit IgM or mouse IgA. M-phi treated with trypsin formed rosettes with IgG2a, but not with IgG1, IgG2b, or IgE. The IgG2a and IgE rosettes were inhibited only by rat IgG2a and IgE, respectively, indicating that they were class specific. IgG1 and IgG2b were not class specific. Apparently rat M-phi have at least three types of Fc receptors: (1) a rat IgG2a-specific, trypsin resistant receptor, (2) a rat IgE-specific, trypsin-sensitive receptor, and (3) a rat IgG1, IgG2b, and heterologous IgG-sensitive, trypsin sensitive receptor. (49 Refs)

## 34. SUBPOPULATIONS OF T-LYMPHOCYTES IN MULTIPLE MYELOMA.

Pezzutto A, Semenzato G, Agostini C, Raimondi R, Gasparotto G
Policlinico, Via Giustiniani 2, 35100 Padova, Italy
Scand J Haematol; 26(4):333-338 1981

The percentage and absolute numbers of T lymphocytes bearing Fc receptor for IgG and IgM were evaluated in 13 patients with multiple myeloma and in a group of controls of the same age range. An increase in the percentage of TG cells was found, whereas TM cell numbers were not different from those of the controls. In order to better define the properties of the TG lymphocytes, their ability to suppress the PWM-induced B cell differentiation was tested in an in vitro experimental assay. TG cells from multiple myeloma exert a suppressor activity as the TG of the controls in this system. The possible interpretation of suppressor T cell increases in these patients is discussed. (Author abstract) (15 Refs)

## 35. T LYMPHOCYTE SUBPOPULATIONS IN THE BONE MARROW AND PERIPHERAL BLOOD OF UNTREATED PATIENTS WITH MYELOMA.

Giustolisi R, Guglielmo P, Rizzo M, Cacciola E
Cattedra di Ematologia, Universita degli Studi di Catania, Via S. Citelli, 95124 Catania, Italy
Ric Clin Lab; 11(2):129-137 1981

T lymphocyte populations were studied in the bone marrow and the peripheral blood of 10 untreated patients (9 men, 1 woman; 50-75 yr old) with multiple myeloma. Total E rosette-forming cell (ERFC) count in the bone marrow was within a normal range in 9/10 patients, while the peripheral blood ERFC was reduced in 9/10. There was a significant decrease of 'high-affinity' (Tha) ERFC in both bone marrow and peripheral blood; 'low-affinity' (Tla) ERFC showed a significant increase in the bone marrow and no changes (compared with control values) in the peripheral blood. These findings indicate that the increase in the Tla (putative suppressor T cells) was absolute in the bone marrow whereas it was relative in the peripheral blood because of a decrease in the Tha level. (36 Refs)

## 36. A COMPARATIVE STUDY OF LYMPHOCYTES IN EFFUSIONS OF PATIENTS WITH TUBERCULOSIS OR MALIGNANT DISEASE.

Falcao RP, Bottura C
Dept. Clinical Medicine, Sch. Medicine, Univ. Sao Paulo, 14100 Ribeirao Preto, Sao Paulo, Brazil
Clin Exp Immunol; 45(1):201-204 1981

The diagnostic value of the determination of the relative distribution of B (SmIg-positive) and T (E rosetting) cells in the blood and in pleural or ascitic effusions was evaluated in 10 patients with tuberculosis and in six with malignant diseases. A higher percentage of T and a lower percentage of B lymphocytes in serous fluids than in peripheral blood was observed for both groups of patients. We conclude that this procedure is valueless in differentiating between tuberculosis and malignant diseases when effusions containing predominantly lymphocytes and devoid of metastatic cells are examined. (Author abstract) (14 Refs)

## 37. MIXED LYMPHOCYTE REACTIVITY IN SPLEEN CELLS FROM F-9 TUMOR-BEARING MICE. I. SUPPRESSOR CELL INDUCTION AND CHARACTERIZATION.

Bluestone JA, Lopez C, Hurtenbach U
Immunology Branch, Building 10, Room 4B-17, NCI, NIH, Bethesda, MD, 20205
Cell Immunol; 62(2):334-340 1981

The immune capacity of spleen cells from F-9 tumor-bearing mice was assessed in a one-way mixed leukocyte culture (MLR) and in MLR mixing experiments. Alloreactivity was found to be significantly depressed in mice bearing palpable tumors. Mixing experiments demonstrated that the reduced alloreactivity was due to suppressor cell activity in the spleens of the tumorous mice. Suppressor cells were characterized as adherent, Ly2+ T cells. This study provides the basis for an analysis of the cell surface antigens on F-9 embryonal carcinoma cells which lead to the induction of suppressor T cells in these mice. (Author abstract) (22 Refs)

## 38. EVIDENCE FOR T CELL NATURE AND HETEROGENEITY WITHIN NATURAL KILLER (NK) AND ANTI BODY-DEPENDENT CELLULAR CYTOTOXICITY (ADCC) EFFECTORS: A COMPARISON WITH CYTOLYTIC T LYMPHOCYTES (CTL).

Fast LD, Hansen JA, Newman W
(c/o Newman) Program in Basic Immunology, Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
J Immunol; 127(2):448-452 1981

Three monoclonal antibodies (Ab) to human T lymphocytes (9.3, 9.6, and 10.2), a monoclonal Ab to the human Ia antigen (7.2), and a monoclonal Ab recognizing a monocyte-associated antigen (OKM1) were used to characterize three cytolytic effector types: CTL, NK, and ADCC. Activity was measured after treatment with Ab plus C. T cell antigen 9.3 was expressed on all CTL but gave only minimal reduction in NK or ADCC activities in the presence of C. T cell antigen 10.2 was expressed on all CTL and, in the presence of C, reduced by one-half the NK or ADCC activities. CTL were heterogeneous in expression of 9.3 and 10.2 antigens on days 5 and 7 of MLC, whereas all CTL were positive on day 9. T cell antigen, closely associated with the E receptor, was found on all CTL and NK cells and the great majority of ADCC effectors. Our finding with 9.6 confirms by independent and more direct means the findings of others that NK and ADCC effectors reside within the sheep rosetting population. Further experiments were performed with Ab in the absence of C. Ab 9.6 was able to partially block CTL and NK activities but not ADCC effectors. Ab OKM1 was unable to block NK or ADCC activities, despite its ability in the presence of C to ablate the majority of NK and ADCC lytic activity. Ab 9.3 was capable of blocking CTL activity but not NK or ADCC activity. Treatment with Ab 10.2 had no blocking activity against CTL, NK, or ADCC effectors. In sum, these results indicate that NK and ADCC effectors express, at least in part, differentiation antigens recognized by three monoclonal Ab to T lymphocytes, thus suggesting that some of these effectors may derive from a T cell origin. Although NK and ADCC effectors were identical based on cell surface phenotype, Ab blocking experiments could distinguish these activities. (Author abstract) (37 Refs)

### 39. THE EPSTEIN-BARR VIRUS IN THE PATHOGENESIS OF POSTTRANSPLANT LYMPHOPROLIFERATIVE DISORDERS.

Hanto DW, Sakamoto K, Purtilo DT, Simmons RL, Najarian JS
Dept. Surgery, Univ. Minnesota, Box 171, Mayo Memorial Building, 420 Delaware St., S. E., Minneapolis, MN, 55455
Surgery; 90(2):204-213 1981

Twelve renal transplant patients with lymphoproliferative disorders (LPDs) were studied. Two clinical patterns were identified: (1) Young patients present with an infectious mononucleosis-like illness with fever, sore throat, and lymphadenopathy soon after transplantation or antirejection therapy. Many organs are ultimately involved, and the clinical course is one of a rapidly fatal LPD. (2) Older patients present a longer time after transplantation with symptoms of solid tumors involving the CNS, oropharynx, liver, or small bowel. The clinical course is slower, but it is progressive and fatal. Morphologicallly these LPDs can all be classified as polymorphic diffuse B-cell hyperplasia (PDBH) or polymorphic diffuse B-cell lymphoma (PBL). Cell marker studies in four patients demonstrated a polyclonal B-cell proliferation. Transition from a polyclonal B-cell proliferation to a monoclonal tumor may occur. Epstein-Barr virus (EBV) specific antibody titers, anticomplement immunofluorescence staining of tumors for the presence of the Epstein-Barr nuclear antigen (EBNA), and EBV complementary ribonucleic acid (cRNA)/deoxyribonucleic acid (DNA) hybridization and vDNA/DNA reassociation analysis implicate EBV as the probable etiologic agent in these disorders. Successful management of these lethal LPDs may depend on discontinuation of immunosuppression and removal of the allograft. Antiviral therapy, however, may prove to be useful. (Author abstract) (19 Refs)

### 40. INTERFERON PRODUCTION BY A HUMAN LYMPHOBLASTOID CELL LINE (DG-75) FREE OF THE EPSTEIN-BARR VIRUS GENOME.

Lazar A, Reuveny S, Minai M, Traub A, Mizrahi A
Biotechnology Dept., Israel Inst. for Biological Res., Ness Ziona 70450, Israel
Antimicrob Agents Chemother; 20(2):151-154 1981

A new lymphoblastoid cell line, DG-75, was investigated for its ability to produce interferon. DG-75 cells, previously shown to be free of Epstein-Barr virus genome and receptors, could be grown in submerged culture and could produce interferon in titers comparable to interferon produced by Namalva cells. The interferon produced was similar in size to the Namalva interferon as determined by gel filtration in Ultrogel AcA54. The DG-75 cells present a new source for large quantities of interferon which may be safer for human use than the Namalva interferon. (Author abstract) (21 Refs)

## CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION

### 41. AUGMENTATION OF NATURAL KILLER CELLS INVOLVES BOTH ENHANCEMENT OF LYTIC MACHINERY AND EXPRESSION OF NEW RECEPTORS.

Gustafsson A, Lundgren E
Dept. Clinical Virology, Univ. Umea, S-901 85 Umea, Sweden
Cell Immunol; 62(2):367-376 1981

A good correlation was found between the sensitivity of six hematopoietic cell lines to natural killing by both unstimulated and interferon (IFN)-stimulated effector cells and the ability of these cell lines to induce interferon among human WBC. Two cell lines (HL 60 and P3HR1) were not sensitive to natural killing by unstimulated effectors (less than 10 lytic units) and did not induce IFN. Augmentation of natural killing by preincubation of effector cells with IFN was found to alter the binding of lymphocytes to HL 60 cells but not K 562 cells. This indicates that the augmentation of natural killer cells by IFN involves both enhancement of the lytic machinery and development of new receptors. (Author abstract) (26 Refs)

### 42. IMMUNOSELECTION AND CHARACTERIZATION OF MOLONEY MURINE LEUKEMIA VIRUS-INFECTED CELL LINES DEFICIENT IN SURFACE GAG ANTIGEN EXPRESSION.

Edwards SA, Fan H
Peptide Biology Lab., Salk Inst., San Diego, CA, 92138
Virology; 113(1):95-108 1981

NIH/3T3 cells infected with Moloney murine leukemia virus (M-MuLV) which were deficient in gag surface antigen were selected by incubation with anti-serum to the major gag virion protein, p30, in the presence of complement. Survivors of the selection were cloned and characterized with respect to intracellular production of gag and env gene products, gag surface antigen expression as revealed by indirect immunofluorescence, and virus production. Nineteen clones tested were all positive for env gene products in cytoplasmic extracts. Seventeen of the 19 were positive for gag gene products, and 2 were negative. The gag-positive clones all produced Pr65gag (the precursor to the internal structural proteins) and they also produced gPr80gag (the precursor to the cell-surface gag antigen). The selected clones were all deficient in the presence of surface gag antigen as measured by immunofluorescent microscopy or flow microfluorimetry, and they all processed Pr65gag to mature p30 more slowly than the parental cells. In addition, all of the surface gag-deficient clones produced virus at a reduced rate. The nature of the defect in one gag-deficient clone was studied by infection of progeny virus onto uninfected NIH/3T3 cells. The resultant cells showed normal gag surface fluorescence and virus production. This suggests that the defect was cellular rather than viral. (Author abstract) (27 Refs)

## 43. THE REQUIREMENT OF IA-POSITIVE ACCESSORY CELLS FOR THE INDUCTION OF TUMOR-SPECIFIC CYTOTOXIC T LYMPHOCYTES IN VITRO.

Yamashita U, Nakamura H
Dept. Immunology, Univ. Occupational and Environmental Health, Sch. Medicine, 1-1 Iseigoaka, Yahatanishiku, Kitakyushu 807, Japan
Cell Immunol; 62(2):425-435 1981

The mechanism for the induction of cytotoxic T cells specific for tumor-associated antigens was studied by using fractionated responder T cells, tumor cells, and accessory cells in vitro. The tumor-specific cytotoxic T cells were induced by culturing immunized spleen cells with the tumor cells in vitro for 5 days. Nylon-column-purified T cells alone did not induce cytotoxic T cells upon culture with tumor cells, but the addition of normal spleen cells as accessory cells did successfully induce the cytotoxic T cells, suggesting that the presence of accessory cells is required for the activation of tumor-specific cytotoxic T cells in vitro. The accessory function was associated with spleen cell populations adheri ng to a plastic dish, a Sephadex G-10 column or a nylon wool column, and was sensitive to anti-Ia serum and C treatment, but was resistant to anti-Ig serum or anti-Thy 1 serum and C treatment, suggesting that the accessory cells are Ia-positive macrophages. Not only syngeneic but also allogeneic macrophages had the accessory function and the allogeneic macrophages were also Ia positive. These results suggest that Ia-positive macrophages play a crucial role in the induction of tumor-specific cytotoxic T cells in vitro. The possible role of Ia-positive accessory cells in the induction of tumor-specific cytotoxic T cells is discussed from the standpoint of cellular interactions. (Author abstract) (32 Refs)

## 44. INTERFERON ENHANCES THE AMOUNT OF MEMBRANE-BOUND BETA2-MICROGLOBULIN AND ITS RELEASE FROM HUMAN BURKITT CELLS.

Fellous M, Bono R, Hyafil F, Gresser I
Groupe de Recherches d'Immunogenetiques de la Transplantation Humaine, INSERM U 93, Hopital Saint-Louis, 2, Place du Dr. Fournier, F75475 Paris Cedex 10, France
Eur J Immunol; 11(6):524-526 1981

Human leukocyte interferon (HuIFN-alpha) increased the amount of beta2-microglobulin on the surface of human Burkitt lymphoma cells (Ramos) and also increased the amount released into the culture medium. The effect was observed 1 hr after addition of IFN. These results suggest that the increase in beta2-microglobulin on the cell surface of IFN-treated cells is not due to a decreased shedding of antigen from the cell surface, nor an 'unmasking' of surface antigen, but rather to an increased synthesis of antigen. (Author abstract) (38 Refs)

## 45. ACTIVATED MACROPHAGES AS EFFECTOR CELLS IN ANTITUMOR DEFENSE.

Vladro MM
P. A. Hertsen Res. Oncological Inst., Moscow, USSR
Vopr Onkol; 27(6):80-89 1981

Literature data on the antitumor effect of activated macrophages (AM) are reviewed. A broad spectrum of agents can induce macrophage activation (MA). BCG-induced MA depends upon the vaccine viability, dosage, route, and number of administrations. Treatment of macrophage membrane with inhibitors of protein synthesis was shown to change macrophage sensitivity to activating agents. Recent studies showed that AM contain a new surface antigen, which was absent on the surface of intact macrophages. AM can have a cytotoxic effect on the syngeneic, as well as on the allogeneic and even xenogeneic tumor cells. Contact lysis is thought to be a chief mechanism of the antitumor effect of AM. Simultaneous injection of tumor cells and AM caused inhibition or complete tumor regression in experimental animals. (119 Refs) (In RUS)

## 46. LY-M19: THE LYB-2 REGION OF MOUSE CHROMOSOME 4 CONTROLS A NEW SURFACE ALLOANTIGEN.

Tada N, Kimura S, Liu Y, Taylor BA, Hammerling Y
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Immunogenetics; 13(6):539-546 1981

Spleen cells from an SJL mouse immunized with 70Z/3 cells, an established pre-B cell line, were fused with cells of the nonsecretor myeloma line NS.1. One established hybridoma cell line (clone K10.6) continuously secreted antibody that recognized a new antigenic specificity tentatively named Ly-m19. This newly found antigen is detectable on both T and B cells. Cytotoxicity assays reveal that 75% of the spleen and lymph-node cells, 35% of bone marrow cells, and 15% of thymus cells reacted with antibody of clone K10.6. Strains expressing the specificity Ly-m19.1 are characterized by negative reactions and include the strains AKR, CE/J, RF/J, GR/A, SJL, P/J, BDP/J, and LG/J. All other strains so far tested are Ly-m19.2. This strain distribution pattern distinguishes Ly-m 19 from any known murine lymphocyte alloantigen, but it parallels the Lyb-2c haplotype. Linkage test of a set of AKXL recombinant inbred strains revealed close linkage of Ly-m19 and Lyb-2 loci on mouse chromosome 4. (Author abstract) (24 Refs)

## 47. EVIDENCE FOR INTERACTION BETWEEN T CELL POPULATIONS OF TUMOR-BEARING AND NORMAL MICE IN IMMUNE SUPPRESSION.

Ingenito GG, Calkins CE
Dept. Microbiology, Thomas Jefferson Univ., 1020 Locust St., Philadelphia, PA, 19107
J Immunol; 127(3):1236-1240 1981

Spleen cells of DBA/2 mice bearing sc implants of the syngeneic tumor L5178Y induce suppression of the in vitro antibody response of normal spleen cells to sheep RBC (SRBC). Cells mediating suppression are detected in the spleens of tumor-bearing mice as early as 24 hr post-implantation but are no longer detected there 15 days post-implantation. These spleen cells are nylon wool nonadherent, sensitive to anti-Thy 1.2 + C and anti-Lyt 1.1 + C, and insensitive to anti-Lyt 2.1 + C treatment. The anti-SRBC response of the unfractionated spleen cells from the tumor-bearing mice is not itself suppressed at the cell numbers used. This along with the finding that suppression occurs in the presence of spleen cells from normal mice suggest that a cell population from the normal mouse spleen is also involved in the suppression. Spleen cells from mice inoculated with irradiated (nonproliferating) L5178Y cells are similarly capable of mediating nonspecific suppression for the same limited period of time after the inoculation. In addition, spleen cells from mice stimulated with several nontumorigenic cellular antigens interact with normal spleen cells to produce suppression. These findings suggest that suppression observed in vitro with spleen cells from these tumor-bearing mice may be the result of antigen-activated cells triggering normal immunoregulatory cells. (Author abstract) (30 Refs)

## 48. QUANTITATIVE APPRAISAL OF H-2 PRODUCTS IN T CELL-MEDIATED LYSIS BY ALLOGENEIC AND SYNGENEIC EFFECTOR CELLS.

Kuppers RC, Ballas ZK, Green WR, Henney CS
Deutsches Krebsforschungszentrum, Im Neunheimer Feld 280, 6900 Heidelberg 1, W. Germany
J Immunol; 127(2):500-504 1981

In this report we attempted to distinguish the amount of the serologically defined H-2 products on target cells necessary for their lysis by either alloimmune cytotoxic T lymphocytes (CTL) or by syngeneic, major histocompatibility complex-(MHC) restricted, CTL. Target cells, which were treated with papain and subsequently modified with TNBS, were examined for their susceptibility to lysis by allogeneic and syngeneic CTL. Lysis of papain-treated cells by both types of CTL decreased in a parallel fashion. The decline in lysis correlated with the loss of serologically defined H-2 antigens from the cell surface. Additionally, a panel of cell lines displaying different amounts of H-2 products were examined for their susceptibility to lysis by both sets of effector cells. As with the papain-treated cells, these H-2 'variants' showed a direct relationship between the amount of H-2 products displayed on their surface and their susceptibility to lysis by both the allogeneic and the syngeneic, TNP-specific, effector cells. Whereas papain treatment caused a decrease in the amount of TNP that could be coupled to the target cells, the 'variant' cell lines displayed comparable amounts of TNP after incubation with TNBS. Moreover, further analysis of the papain-treated target cells revealed that it was the amount of the H-2 products, rather than the amount of TNP, which was the limiting variable for recognition by syngeneic CTL. These findings collectively suggest that regardless of whether MHC products act as the restricting element in lytic interactions (as with MHC-restricted TNP-specific syngeneic CTL) or as the substrate for lytic attack (as with alloimmune specific CTL) the quantitative requirements for MHC products are similar. (Author abstract) (23 Refs)

## 49. SPECIFICITIES OF KILLING BY T LYMPHOCYTES GENERATED AGAINST SYNGENEIC SV40 TRANSFORMANTS: CROSS-REACTIVITY OF THE H-2KBM1 THROUGH KBM4 H-2 MUTANT ALLELES IN KB-RESTRICTED SV40-SPECIFIC KILLING.

Whitmore AC, Gooding LR
Dept. Microbiology and Immunology, Div. Immunology, Duke Univ. Medical Center, Durham, NC, 27710
J Immunol; 127(3):1207-1211 1981

SV40-specific cytotoxic T lymphocytes (CTL) produced in H-2Kb recombinant mice do not kill SV40-transformed mouse embryo fibroblast (MEF) targets from strains bearing the histocompatibility mutations H-2Kbm1, Kbm2, Kbm3, and Kbm4 although CTL from SV40-immune H-2db-bearing recombinant mice kill all of the SV40-transformed mutant cell lines with similar kinetics. Similarly, B6.C-H-2bm1, B6.C-H-2bm2, B6-H-2bm3, and B6.C-H-2bm4 spleen cells immunized with syngeneic SV40-transformed cell lines do not kill recombinant transformed cell lines bearing H-2Kb antigens whereas the same immune cell populations will kill H-2Db-bearing recombinant targets with similar dose-response relationships. Although SV40-transformed cell lines do not cross-react with H-2Kb-bearing targets as restriction elements for SV40-specific CTL, allogeneic Kb-specific CTL displayed significant killing of all mutant cell lines, as did allogeneic Db-specific CTL. Apparently, the functional cross-reactivity of H-2Kb-encoded molecules as restriction elements for SV40-specific T cell-mediated immunity is effectively abolished by the bm1 through bm4 series of mutations at H-2Kb while a significant proportion of the determinants recognized by allogeneic Kb-specific immune CTL are left unmodified. Two possible explantations could account for these findings. Either (1) the mutations have altered the ability of Kb-encoded cell surface elements to form an immunogenic complex with SV40-specific cell surface antigens and the mutant cell lines neither generate K-end-restricted populations of CTL nor do they serve as targets for K-end-restricted killing, or (2) H-2Kb mutant antigens form immunogenic complexes with SV40 antigens but the populations of CTL generated by syngeneic SV40 immunization are so much more specific than alloimmune CTL (or fewer clones of CTL are activated in syngeneic immunity) that little or no cross-reactivity can be seen between these 4 H-2 mutations and the 'wild-type' H-2Kb restriction element. (Author abstract) (31 Refs)

## 50. A MODEL OF T-CELL UNRESPONSIVENESS USING THE MALE-SPECIFIC ANTIGEN, H-Y.

Simpson E, Chandler P, Pole D
Transplantation Biology, Clinical Res. Centre, Watford Road, Harrow, Middlesex HA13UJ, England
Cell Immunol; 62(2):251-257 1981

The immune response to H-Y, a simple cell surface determinant, is clearly extraordinarily complex. It is controlled by H-2 genes mapping at the K and D loci, as well as by I-region genes. It is manifest by skin graft rejection, H-2 restricted cytotoxicity, delayed-type hypersensitivity, and host-vs-graft responses. Suppressor cells may very well be responsible both for neonatally induced tolerance and for nonresponsiveness in adult mice of certain haplotypes. The in vivo responses of graft rejection and DTH have so far been seen only in mice of the H-2b haplotype whereas the in vivo host-vs-graft response and the in vitro cytotoxic response have been found in a wider range of H-2 types, although a variety of strategies need to be used in order to reveal responsiveness in some haplotypes. We do not yet know which of these responses are important in antitumor immunity, but the findings so far have alerted us to the possibility that MHC antigens of the responder are very important and that certain refractory states of nonresponsiveness can be reversed. Understanding of the underlying mechanisms and cell-cell interaction during the generation of immune responses is vital for a rational approach to the control of antiallograft and antitumor responses. (Author abstract) (30 Refs)

## 51. MONCOLONAL ANTI-GP70 ANTIBODIES CAUSE IN VIVO REDUCTION OF FRIEND VIRUS INFECTIOUS CENTERS IN LEUKEMIC SPLEENS (MEETING ABSTRACT).

Chesebro B, Britt WJ
Laboratory of Persistent Viral Diseases, Rocky Moutain Laboratories, Hamilton, MT
RNA Tumor Viruses, May 20-24, 1981, Cold Spring Harbor, New York Cold Spring Harbor Laboratory 294 pp., 1981.

Monoclonal antibodies which treated with gp70, p15 and p15E proteins of Friend virus (FV) were obtained from hybridomas derived from spleen cells of mice recovering from Friend virus-induced erythroleukemia. Two antibodies appeared to have the Friend-Moloney-Rauscher pattern of specificity. One of these was specific for gp70 and the other for p15. Seven other anti-gp70 antibodies and 1 anti-p15 were restricted in reactivity to Friend and Rauscher viruses, and some Friend-MCF viruses. Two to four days after inoculation of monoclonal antibody, three different IgG2a anti-gp70 antibodies caused a 10-to 1000-fold reduction in the number of spleen cells scoring as F-murine leukemia virus infectious cen-

ters without reducing the number of leukemic cells containing cytoplasmic viral antigens. Monoclonal IgG2a or IgG2b anti-p15 and IgM anti-gp70 antibodies did not cause this effect in spite of the fact that these antibodies could lyse FV leukemia cells or FV-infected cells in vitro in the presence of complement. One possible mechanism for the reduction of infectious centers by anti-gp70 antibodies was decreased release of infectious virus from cells as a result of antibody-induced modulation of cell surface gp70 molecules. However, the short time interval between exposure to antibody and observation of decreased infectious centers would appear to make this mechanism less likely. These results appeared to mimic the effect of the Rfv-3 gene seen in (B10.A X A) F1 mice 30-60 days after FV inoculation, where virus release was markedly reduced in spite of continued massive splenomegaly. (no Refs)

### 52. PRESENCE OF RECOMBINANT MULV LIKE GLYCOPROTEIN IN VIRUS FREE MOUSE LYMPHOMAS: A MODEL FOR AUTOSTIMULATORY BLASTOGENESIS (MEETING ABSTRACT).

Fischinger P, Thiel H, Ihle J, Dunlop N
National Cancer Institute, Frederick, MD
RNA Tumor Viruses, May 20-24, 1981, Cold Spring Harbor, New York. Cold Spring Harbor Laboratory 294 pp., 1981.

The NIXT x-ray induced T-cell lymphoma line from Swiss mice had no virus or viral antigens detected by standard infectious assays or by radioimmunoassay or immunofluorescence (IFA) assays. However 5-10% of these cells in log phase of growth expressed on their surface in IFA an antigen reactive with anti VL-3 Rad LV gp70 serum which was primarily reactive with recombinant (RM) Murine leukemia viruses (MuLV). Ecotropic MuLV replicated in NIXT cells, but RM-MuLV could neither replicate nor enter these cells as seen by exclusion of Mouse sarcoma virus (MSV) (RM-) pseudotypes. Radioimmune precipitation tests of surface labeled cells with both anti VL-3 gp70 and other MuLV group reactive gp70 sera demonstrated a gp70, which by peptide maps was shown to be of the RM-MuLV class. This antigen may have a model role in leukemogenesis, because T lineage cells exist which have receptors for RM gp70, which when bound could act as a blastogenesis signal. The expression of permuted gp70's in the absence of virus on cell with receptors could result in continued cycles of replication. Thus, besides the direct onc gene product model, and the indirect promoter insertion model, one can postulate an alternate hypothesis based on the calls for clonal expansion of a receptor defined cell subpopulation. (no Refs)

### 53. IMMUNOLOGIC ASPECTS OF CANCER.

Oettgen HF
Clinical Immunology Service, Memorial Sloan-Kettering Cancer Center, New York, NY
Hosp Pract; 16(7):85-88,90,93-95 1981

Current research in the field of tumor immunology is reviewed with special emphasis on the identification of tumor-specific antigens. In vitro techniques demonstrated that tumors and leukemias induced by oncornaviruses express the transplantation antigens. Tumors induced by chemical antigens or oncogenic viruses were found to vary in their ability to render mice immune to subsequent challenge with the same tumor. Human tumor-specific antigens defined by heterologous sera were shown to be differentiation antigens. An autologous typing of greater than 200 melanoma patients revealed three classes of surface antigens, ie antigens restricted to the autologous tumor and not detectable on autologous normal cells; shared tumor antigens, expressed by autologous as well as by some allogeneic tumors of similar or different origin; and antigens widely distributed on autologous, allogeneic, and xenogeneic normal and malignant cells. Development of serologic typing systems for defining cell surface antigens of melanoma and other cancers provided the basis for assaying a number of different melanoma vaccines. (5 Refs)

## EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS

### 54. INDUCTION OF COMPLEMENT RECEPTOR EXPRESSION IN CELL LINES DERIVED FROM HUMAN UNDIFFERENTIATED LYMPHOMAS. I. MODE OF ACTION OF THEOPHYLLINE AND INHIBITION BY CERTAIN PURINES.

Magrath I, Freeman C, Novikovs L
Pediatric Oncology Branch, NCI, Bethesda, MD, 20205
J Immunol; 127(3):1034-1038 1981

We have demonstrated that theophylline will induce complement-receptor expression, detected by EACM rosette formation, in three cell lines (EW36, CA46, and JD38) derived from Burkitt's lymphoma and the closely related undifferentiated lymphoma. In the present report dealing with two of these lines , we show that several methylated xanthines will induce receptor expression but that other purines or purine derivatives will not. However, purine, adenine, and adenosine inhibit the inducing effect of theophylline. Complement receptor induction is also dependent upon RNA synthesis, since actinomycin D (AD) will delay, modify, or totally inhibit receptor induction, depending upon the time of addition after theophylline and the duration of exposure. Essentially similar effects were achieved by adding AD or removing theophylline at any given time point during the first 14 hr. After 24 hr, however, whereas removal of theophylline resulted in a decline in the fraction of EACM rosette-forming cells, addition of AD did not have any effect on receptor expression, indicating that maintenance of receptors does not require continued RNA synthesis. Although purine, adenine, adenosine, and papaverine were incapable of inducing complement receptors, each was able to replace theophylline in the maintenance of receptor levels, further supporting the probability that induction and maintenance of receptors have separate mechanisms. Dibutyryl cyclic 3,5-AMP neither induced receptors, nor was it able to substitute for theophylline in the maintenance of receptors. This does not rigorously exclude the participation of cyclic nucleotides, but strengthens the likelihood that the processes of receptor induction and maintenance are not mediated by cAMP. (Author abstract) (28 Refs)

## 55. INDUCTION OF COMPLEMENT RECEPTOR EXPRESSION IN CELL LINES DERIVED FROM HUMAN UNDIFFERENTIATED LYMPHOMAS. II. CHARACTERIZATION OF THE INDUCED COMPLEMENT RECEPTORS AND DEMONSTRATION OF THE SIMULTANEOUS INDUCTION OF EBV RECEPTOR.

Magrath I, Freeman C, Santaella M, Gadek J, Frank M, Spiegel R, Novikovs L
Pediatric Oncology Branch, NCI, Bethesda, MD, 20205
J Immunol; 127(3):1039-1043 1981

We have studied the specificity of complement receptors induced by theophylline in two cell lines derived from undifferentiated lymphomas, one of Burkitt's type, and compared it to that of complement receptors in other cell types. Both C3b and C3d receptors were induced. The induced C3b receptor differed from the C3b receptor of mature normal lymphocytes, polymorphonuclear leukocytes and the cells of a nodular lymphoma in two respects. Firstly, it bound C3b much less avidly (by a factor of several hundred-fold) and secondly, we were unable to demonstrate C4b binding. EBV receptors were induced at the same time as complement receptors, and permitted the conversion of a greater fraction of cells to EBNA positivity after experimental infection with EBV. The induction of receptors was not associated with a change in the fluidity of the plasma membranes and our data do not favor a different orientation of induced receptors within the membrane as compared to receptors of other cell types - a potential explanation for the different specificities. Our findings are consistent with the possibility that the complement receptors of lymphocyte precursors differ from those of mature lymphocytes. (Author abstract) (20 Refs)

## 56. IMMUNOTHERAPY OF MURINE LEUKEMIAS BY MONOCLONAL ANTIBODY. I. EFFECT OF PASSIVELY ADMINISTERED ANTIBODY ON GROWTH OF TRANSPLANTED TUMOR CELLS.

Kirch ME, Hemmerling U
Dept. Immunochemistry, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
J Immunol; 127(2):805-810 1981

The objective of the present study was to establish a model system for the evaluation of passive immunotherapy of murine leukemias. Monoclonal antibodies directed at T lymphocyte differentiation antigens (Thy 1 and Lyt 2) were tested for their effect on tumors that were grown in hosts congenic for the target antigen. Tumor challenges were selected that were at least 500 x the dose that was lethal in 50% of untreated controls. The A strain leukemia, ASL.1, was transplanted sc into A/Thy 1.1 congenic hosts. Ip administration of anti-Thy 1.2 monoclonal antibodies of the IgG3 and IgM classes reduced tumor growth. Up to 90% of the mice receiving antibody of the IgG3 subclass failed to develop tumors, whereas IgM antibodies prolonged survival time, but the mice eventually died of tumors. Antibody was most effective if administered within 24 hr of tumor inoculation; delay of antibody injection for 48 hr prolonged host survival but did not eradicate cells at the injection site or prevent metastases. The C57BL/6-derived tumors, ERLD and EL4, were evaluated for susceptibility to treatment with antibody directed at the Lyt 2.2 alloantigen using the protocol that was effective in treating ASL.1. Monoclonal antibody of the IgG2a subclass was effective in the case of C57BL/6/Lyt 2.1 congenic mice bearing ERLD, but caused a decrease in survival time of mice bearing the transplanted EL4 tumor. Thus, antibody of the appropriate immunoglobulin subclass can be effective in controlling tumor growth if administered in the optimal treatment regimen, but inherent features of the tumor cell ultimately determine whether abrogation or enhancement of growth will occur. (Author abstract) (47 Refs)

## 57. DIFFERENTIAL EFFECT OF INTERFERON ON THE EXPRESSION OF TUMOR-ASSOCIATED ANTIGENS AND HISTOCOMPATIBILITY ANTIGENS ON HUMAN MELANOMA CELLS: RELATIONSHIP TO SUSCEPTIBILITY TO IMMUNE LYSIS MEDIATED BY MONOCLONAL ANTIBODIES.

Imai K, Ng AK, Glassy MC, Ferrone F
Dept. Molecular Immunology, Scripps Clinic and Res. Foundation, 10666 North Torrey Pines Road, La Jolla, CA, 92037
J Immunol; 127(2):505-509 1981

Incubation of cultured human melanoma cells with human leukocyte interferon did not change the expression melanoma-associated antigens (MAA) recognized by monoclonal antibodies and of Ia -like antigens but significantly increased the expression of HLA-A,B antigens and Beta2-microglobulin (B2-u). The effect is dependent on the dose of interferon and on the incubation time. Interferon-treated melanoma cells showed an increased susceptibility to lysis mediated by monoclonal antibodies to HLA-A,B antigens and to human B2-u; on the other hand, interferon-treated melanoma cells did not change in their susceptibility to murine natural (NK) cell lysis and to immune lysis mediated by monoclonal antibodies to MAA and to Ia-like antigens, and they displayed a reduced susceptibility to human NK cell lysis. Therefore, the increased susceptibility of interferon-treated melanoma cells to lysis mediated by anti HLA-A,B and anti B2-u monoclonal antibodies is likely to reflect the increase in cell surface expression of the corresponding antigens. (Author abstract) (29 Refs)

## 58. LEUKEMOGENIC PROPERTIES OF AKR DUALTROPIC (MCF) VIRUSES: AMPLIFICATION OF MURINE LEUKEMIA VIRUS-RELATED ANTIGENS ON THYMOCYTES AND ACCELERATION OF LEUKEMIA DEVELOPMENT IN AKR MICE.

O'Donnell PV, Stockert E, Obata Y, Old LJ
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Virology; 112(2):548-563 1981

The late preleukemic period in AKR mice (6-8 mo of age) is characterized by amplified expression of murine leukemia virus (MuLV)-related cell surface antigens on thymocytes. Analysis of thymic biopsies of preleukemic AKR mice at 180 days of age showed that antigen amplification was prognostic of spontaneous leukemia development within approx 100 days. In the present study we have investigated the viral basis of this preleukemic change in AKR thymus. Cloned isolates of ecotropic, xenotropic, and dualtropic MuLV that were derived from preleukemic or leukemic AKR thymus were tested by intrathymic injection of young AKR mice to determine which of the three classes of MuLV could induce antigen amplification, and, subsequently, accelerate leukemia development in the same animal. Only dualtropic MuLV exhibited these two activities in vivo. Considerable heterogeneity was observed among the 13 dualtropic MuLV isolates examined. In vitro three distinct serological phenotypes could be recognized on the basis of expression of MuLV gag gene-coded antigens GCSA and MuLV env gene-coded antigens GIX, G(RADA1), G(ERLD), and G(AKSL2) on the surface of infected cells. Virus isolates also differed in (i) relative ecotropic-xenotropic host range (dualtro-

pism) as assayed by ratios of infectious titers on mouse and mink cells, (ii) induction of mink cell foci (MCF), and (iii) infectivity for NIH/3T3 cells.In vivo the two activities of antigen amplification and leukemia acceleration could be dissociated and thus represent distinct virus phenotypes. Seven isolates of dualtropic MuLV induced antigen amplification; these viruses encoded GIX, G(ERLD), and G(AK SL2) antigens, were MCF inducing, had SC-1/mink titer ratios of 0.4 or greater, and were infectious for NIH/3T3 cells. Only three of these virus isolates (MCF 247, MCF 69L1, and MCF 13) accelerated leukemia development. Analysis of dose-response relationships and kinetics of virus-induced antigen amplification by MCF 69L1 virus implicated virus infection of thymocytes in the preleukemic change. Moreover, the level of MuLV antigen expression on thymocytes at approx 1 mo postinjection of MCF 69L1 virus correlated directly with development of early leukemia. It is apparent that leukemia development in young AKR mice which can be induced experimentally by intrathymic injection of cloned isolates of dualtropic MuLV exhibits the hallmarks of spontaneous disease in this strain and thus can serve as a useful model for study of thymic leukemogenesis in mice. (Author abstract) (55 Refs)

## 59. INDUCTION OF SEVERAL NEW ANTIGENS, INCLUDING A T CELL-ASSOCIATED ANTIGEN, FOLLOWING CONVERSION OF THE EBV-NEGATIVE B CELL LINE RAMOS TO EHRB-RAMOS BY EPSTEIN-BARR VIRUS.

**Rosenthal KS, Shuman H, Strominger JL**
**Sidney Farber Cancer Inst., Harvard Medical Sch., Boston, MA, 02115**
**J Immunol; 127(2):746-754 1981**

Heteroantisera prepared against EHRB-RAMOS cells and then absorbed extensively with the syngeneic EBV-negative cell line RAMOS recognized a membrane antigen present on EHRB-RAMOS but not on RAMOS cells. The binding of the sera, anti-EHRB, was measured by several immunologic techniques that detect cell surface molecules, including cytotoxicity, immunofluorescence, and the 125I-staph protein A assay. Triton X-100 extracts of plasma membranes prepared from EHRB-RAMOS competed for the binding of anti-EHRB on EHRB-RAMOS, as measured by the staph protein A assay, whereas extracts of RAMOS membranes did not. The anti-EHRB sera also recognized the EHRA-RAMOS cell line, but binding of anti-EHRB to other EBV-converted RAMOS lines--African Burkitt lymphoma lines, newly established and well established lymphoblastoid cell lines, and EBV producer cell lines--was undetectable. The anti-EHRB sera recognized 4 T cell lines established from T cell leukemias, including CEM, HSB, YT4E, and MOLT 4. In addition, an anti-CEM serum, prepared in this laboratory, recognized the EHRB-RAMOS cells. Absorption of the serum with peripheral blood lymphocytes removed the activity of anti-EHRB to both the T cell lines and to EHRB-RAMOS, as detected by immunofluorescence using the fluorescence-activated cell sorter. The EHRB-RAMOS cells still retained B cell characteristics, since they expressed p29, 34, an antigen found on normal peripheral B cells, and did not rosette with sheep RBC. The anti-EHRB sera and anti-CEM sera were further characterized by radioimmunoprecipitation of 35S-methionine-labeled proteins of EHRB-RAMOS, RAMOS, YT4E, CEM, and HSB. Anti-E HRB recognized polypeptides of 16, 32, and 35 x 10(3) daltons on EHRB-RAMOS and 85 x 10(3) daltons on EHRB-RAMOS, CEM, HSB, and YT4E. Anti-CEM recognized polypeptides of 95 to 130 x 10(3) daltons expressed on the T cells and EHRB-RAMOS. These polypeptides were absent from or expressed to a much less extent on RAMOS. Thus conversion of RAMOS by EBV to the EHRB-RAMOS B cell line was associated with the appearance of several different antigens, some of which were also present on 4 T cell lines and on peripheral blood lymphocytes (as evidenced by absorption). (Author abstract) (42 Refs)

## 60. CHARACTERIZATION OF SERUM-INDUCED ALTERATIONS IN THE CYCLIC AMP PATHWAY IN S49 LYMPHOMA CELLS.

**Darfler FJ, Hughes RJ, Insel PA**
**Div. Pharmacology, Dept. Medicine, Univ. California, San Diego, La Jolla, CA, 92093**
**J Biol Chem; 256(16):8422-8428 1981**

We have grown the S49 lymphoma cell line in a serum-free, chemically defined medium which contains casein, insulin, transferrin, testosterone, and linoleic acid. When grown in this medium, wild type S49 cells display a two- to three-fold increase in hormonal (beta-adrenergic, prostaglandin E1) and nonhormonal (cholera toxin) stimulation of cAMP accumulation compared to cells grown in 10% horse serum. Wild type cells grown in serum-free medium contained 30% more beta-adrenergic receptors than did serum-grown cells, although the affinity of the receptors for [3H]dihydroalprenolol was unchanged. The S49 variants, UNC and kin-, failed to show the alterations in cholera toxin- or isoproterenol-stimulated cAMP accumulation that were observed with wild-type cells. 125I-labeled cholera toxin binding studies showed no change in the number or affinity of cholera toxin receptors in wild type or kin- cells grown under the two conditions. In cell homogenates, wild type cells grown in serum-containing medium had 28-45% higher activity of cyclic nucleotide phosphodiesterase than did cells grown in serum-free medium. Growth with or without serum produced no change in the Km values (14 and 0.25 uM, respectively, for the 2 forms) of phosphodiesterase in these cells. Basal, NaF-, Gpp(NH)p-, and isoproterenol plus GTP-stimulated adenylate cyclase activities were similar in crude plasma membrane preparations from serum-free and serum-grown wild type cells. Horse serum contained a nondialyzable (greater than 8,000 daltons), nonlipid factor which depressed the isoproterenol-stimulated cAMP accumulation of wild type S49 cells and which required 3-4 hr to produce this effect. This factor appears to act via the nucleotide-coupling unit of the adenylate cyclase system and protein kinase, and ultimately results in an increase in cyclic nucleotide phophodiesterase activity. We suggest that studies of the cAMP pathway in S49 cells should ideally be carried out under the less perturbing conditions offered by serum-free medium. (Author abstract) (35 Refs)

## 61. THE ALVEOLAR MACROPHAGE: IMMUNE DERANGEMENT AND ASBESTOS-RELATED MALIGNANCY.

**Kagan E**
**Dept. Pathology, Georgetown Univ. Sch. Medicine, 3900 Reservoir Road N. W., Washington, DC, 20007**
**Semin Oncol; 8(3):258-267 1981**

The role of the alveolar macrophage and immunologic mechanisms in the pathogenesis of asbestosis are highlighted and the significance of these observations against a background of asbestos-associated immune derangement was evaluated. An attempt is made to assess the relevance of these findings and to the development of certain asbestos-associated malignancies. Evidence suggesting a pathogenetic role of the alveolar macro-

phage in asbestosis is reviewed. No immune response to alveolar macrophage cell surface antigens has yet been demonstrated in asbestosis, although there are several immune reactions that occur at the surface of asbestos-exposed, but not alveolar macrophages that may include an immune response directed against components of the cell surface. In workers exposed to asbestos for 9-28 yr but without asbestosis, levels of IgA, IgG, and IgM were significantly higher than workers with exposure of less than 2 yr. Striking derangements of immunologic function have been observed in subjects with asbestosis. In patients with asbestos-related cancers, no conclusions can be made because of the limited data. The possible contribution of asbestos-related immune derangement to the development of malignancy is discussed. Asbestos-associated immune dyscrasias are discussed and future perspectives in this field are mentioned. (99 Refs)

## 62. TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE ACTIVITIES AND GLUCOCORTICOID RECEPTORS IN LEUKAEMIA.

**Sasaki R, Takaku F, Aoki T, Bollum FJ, Saito T, Dan S**
**Dept. Haematology, Jichi Medical Sch., 3311-1 Yakushiji Minamikawachi-Machi, Kawachigun, Tochigi 329-04, Japan**
**Br J Cancer; 44(1):63-67 1981**

The relation between terminal deoxynucleotidyl transferase (TdT) activity, glucocorticoid (GC) receptors and the effect of vincristine-prednisolone (VP) therapy on fresh leukemia cases was examined. Five of six TdT+ leukemias showed high levels of GC receptors and a favorable response to VP therapy, whereas one acute lymphoblastic leukemia and three of chronic myelogenous leukemia cases in blast crisis with no TdT activity showed low level of GC receptors and poor response to VP therapy. Significant correlation ($r = 0.821$, $p$ less than 0.01) was observed between TdT activity and the number of GC receptor sites in these cases. Chi square test showed significant difference ($p$ less than 0.01) between TdT+ and TdT- leukemias in the effect of VP. A significant difference ($p$ less than 0.01) was also observed between VP-effective and ineffective leukemias in the number of GC-receptor sites by unpaired t test. Therefore GC receptors may b e responsible for the effect of VP on TdT+ leukemias. (Author abstract) (18 Refs)

## 63. INVESTIGATIONS OF UNSPECIFIC IMMUNE REACTIVITY IN PATIENTS WITH HEAD AND NECK CARCINOMA.

**Bier J, Nicklisch U**
**Abteilung fur Kiefer- und Plastische Gesichtschirurgie,, Universitatsklinikum Steglitz Freie Universitat Berlin, Hindenburgdamm 30, D-1000 Berlin 45, W. Germany**
**Arch Otorhinolaryngol (NY); 232(2):145-163 1981**

Nonspecific immune reactions in thirty patients with squamous cell carcinoma of the head and neck were compared with reactions in thirty healthy controls. Patients included 15 males and 15 females, aged 27-81 yr, with an av age of 59 yr. In vitro assays measured the blastogenic stimulation of lymphocytes by the mitogens phytohemagglutinin (PHA), Concanavalin A (ConA), and pokeweed mitogen (PWM). Absolute and percentage values for T-rosette-forming lymphocytes were obtained. Delayed hypersensitivity to dinitrochlorobenzene (DNCB) was measured by skin tests. Parameters were determined in patients at 4-wk intervals for a period of 1 yr or until death. Patients were treated by surgery, chemotherapy with Bleomycin and Methotrexate, and radiation therapy. Follow-up continued for 5 yr. Tumor patients before treatment showed marked reduction of immune response, when compared to controls. A further, temporary reduction occurred during treatment. No correlation could be demonstrated between tumor stage and nonspecific immune reactivity. No useful statement could be made regarding nonspecific immune reactivity in patients with squamous cell carcinoma of the head and neck. (37 Refs) (In GER)

## 64. EPSTEIN-BARR VIRUS CO-RECONSTITUTED WITH SENDAI VIRUS ENVELOPES INFECTS EPSTEIN-BARR VIRUS-RECEPTOR NEGATIVE CELLS.

**Shapiro IM, Klein G, Volsky DJ**
**Dept. Tumor Biology, Karolinska Institutet, Box 60400, S-104 01 Stockholm, Sweden**
**Biochim Biophys Acta; 676(1):19-24 1981**

Epstein-Barr virus (EBV) was co-reconstituted with Sendai virus envelopes. The reconstituted 'hybrid' virus could bind and penetrate into EBV-receptor negative cells. Using this approach, T-cell-derived human and mouse leukemia cells, human T-lymphocytes and mouse spleen cells were successfully infected as judged by the induction of EBV-determined antigens and stimulation of DNA synthesis. The T-cell-derived human leukemia line Molt-4, that can absorb EBV but without virus penetration, could be also infected by the reconstituted EBV. (Author abstract) (27 Refs)

## 65. CIMETIDINE PROTECTION AGAINST LETHAL TUMOR CHALLENGE IN MICE.

**Gifford RR, Voss BV, Ferguson RM**
**Box 161, Mayo Memorial Building, 420 Delaware St., S. E., Minneapolis, MN, 55455**
**Surgery; 90(2):344-351 1981**

Cimetidine, a histamine type-2 receptor antagonist, has been shown to augment proliferative responses of lymphocytes in man and mouse and to increase in vitro-generated murine cell-medi ated cytotoxicity. It has been suggested by others that histamine receptors are involved in modulating the immune response through mediation of suppressor cell function. We have previously described a murine tumor model in which suppressor function increases with advancing tumor burden. We now have examined the in vivo effect of cimetidine on survival in this tumor-bearing murine model. Cimetidine was administered in the drinking water to C57BL/6 mice after an ip injection of an LD90 dose of EL4 tumor cells. The survival rate was noticeably improved (56%) with an optimal dose of cimetidine (100 mg/kg/day) after 30 days, compared to that of water-treated control mice (10%). This protective effect was present with young (2 mo old) as well as older (8 mo old) mice. Rechallenge of cimetidine-treated survivors with a 6x LD100 tumor dose and continuation of cimetidine produced a 33% survival rate. Comparison of cimetidine (100 mg/kg/day) with different doses of diphenhydramine (histamine type-1 antagonist) showed the protective effect to be more type-2 specific. The mechanism of action of cimetidine remains unclear, but based on this work and work by others, we think that cimetidine probably modulates suppressor cell function. Cimetidine may have potential as an immunomodulator. (Author abstract) (21 Refs)

## 66. IMMUNE RESPONSE TO A SOLUBILIZED MEMBRANE ANTIGEN OF THE MURINE LEWIS LUNG CARCINOMA.

McKolanis JR
West Virginia University, Morgantown, WV
Diss Abstr Int (B); 41(12):4392-B 1981

The xenogeneic and syngeneic immune reactivities to a tumor associated membrane antigen (TAMA) of the spontaneous C57B1/6 murine Lewis lung (LL) tumor were established. The antigen was first solubilized from tumor cell membranes using the detergent Triton X100. Xenogeneic rabbit antibody raised to the Triton solubilized antigen identified the antigen on the surface of tumor cells by means of a solid phase radioimmunoassay. Results show that paraformaldehyde fixed LL tumor cell bind 120 percent more xenogeneic antibody than syngeneic control cells. A comparison of antisera adsorbed with syngeneic control or LL cells shows that control adsorbed antiserum binds 160 percent more efficiently than LL adsorbed antiserum. The difference is due to antibody directed specifically toward a unique TAMA on the surface of LL tumor cells. This antibody is adsorbed by LL cells but not by control cells. Hyperimmune syngeneic antiserum to the LL Triton solubilized antigen was also tested against LL tumor cells to determine if the syngeneic host can amount an immune response to the antigen. At a 1:10 antibody dilution LL tumor cells bind 56 percent more antibody than control cells and 80 percent more antibody than spleen cells. The Triton solubilized LL-TAMA was shown to have a mol wt of 2 x 10(5) daltons and a isoelectric point of 4.7. Xenogenic antibody injected intraperitoneally into tumor bearing mice was identified on the surface of tumor cells indicating the antibody binds to tumor cells in vivo. Pretreatment of tumor cells with xenogeneic antiserum was shown to inhibit growth of the tumor as compared to control mice. Also, specific xenogeneic and syngeneic antibody immunotherapy, begun six days after tumor challenge were able to inhibit growth of the tumor as compared to controls. (no Refs)

## 67. CYCLASES IN NORMAL AND LEUKEMIC LYMPHOCYTES (MEETING ABSTRACT).

Carpentieri U, Minguell JJ, Gardner FH
Departments of Pediatrics and Internal Medicine, University of Texas Medical Branch, Galveston, TX
Pediatr Res; 15(4,Part2):575 1981

Persistent low level of cyclic (c)-AMP and persistent high level of cGMP (guanosine monophosphate) in leukemia lymphocytes suggest a modified activity of the cyclases which synthetize them. Soluble and particulate guanylate cyclase (GC) and adenylate cyclase (AC) activities were studied in normal B-enriched and T-enriched lymphocytes, in lymphocytes of children with acute lymphocytic leukemia (ALL) and adults with chronic lymphocytic leukemia (CLL). GC activity was greater in normal T than B cells increased little with isoproterenol and prostaglandins stimulation, and much more with sodium azide and dehydroascorbic acid (DHA) stimulation. GC activity was greater in both types of leukemic lymphocytes and was insensitive to stimulation with DHA and sodium azide. Particulate AC activity was greater in normal B than T cells and increased in both after stimulation with isoproterenol and prostaglandins. In leukemic lymphocytes AC showed depressed activity and was insensitive to stimulation. These findings suggest that circulating T cells are more actively cycling or functioning than circulating B cells. They also suggest a derangement of the activity of both cyclases and/or their receptors in leukemic cells: this derangment may be a cause of leukemic cell escape from their microenvironment control. (no Refs)

## 68. ASYMPTOMATIC DEXAMETHASONE NON-SUPPRESSIBLE ACTH AS A TUMOR MARKER (MEETING ABSTRACT).

Varsano-Aharon N, Urivetzky M
Division of Adult Endo., L. I. Jewish-Hillside Medical Center, North Hyde Park, NY, 11042
63rd Annual Meeting of the Endocrine Society, June 17-19, 1981, Cincinnati, Ohio. The Endocrine Society 385 pp., 1981.

We have exploited the presumed autonomy of tumor ACTH production and measured ACTH in plasma under conditions of dexamethasone suppression as a means of separating the pituitary from the ectopic product. An antiserum with N-terminal specificity known to detect all currently described ACTH prohormonal forms was used. Plasma and urinary cortisol measurements were used as in-vivo assay for ACTH biological activity. A dissociation of immunological from biological activity in the form of a high ACTH/cortisol ratio was interpreted as evidence of circulating ectopic ACTH. We have studied 87 patients with a variety of epithelial and lymphatic tumors without the clinically recognizable syndrome of ectopic hormone production. Patients with benign tumors and noncancerous proliferative conditions were studied as matched controls. Random ACTH and cortisol levels were determined under basal conditions and following 2 days of standard high-dose dexamethasone suppression. The random ACTH levels in the control groups was indistinguishable from those of 24 healthy adults. The basal ACTH levels of cancer patients showed a wide scatter and a mean of 2 standard deviation over the mean for controls. The highest levels were associated with amine-precursor uptake decarboxylation (APUD) tumors and epidermoid lung cancer. Significantly better discrimination between cancer patients and controls was achieved with dexamethasone administration. Normals and controls showed maximal suppression of both ACTH and cortisol with ACTH/cortisol ratio unchanged. A total of 32% of the cancer patients had ACTH non-suppressibility, but maximal cortisol suppression. The ACTH cortisol ratio increased from a random mean of 2.57 +/-3.31 to 21 +/-15. Two patients with APUD tumors and random levels in excess of 250 pg/ml showed high degree of ACTH suppressibility. (no Refs)

## 69. GLUCOCORTICOID RECEPTORS AND GLUTAMINE SYNTHETASE IN PATIENTS WITH ACUTE LYMPHATIC LEUKEMIA (MEETING ABSTRACT).

Marchetti P, Ranelletti FO, Natoli V, Longo P, DeRossi G, Iacobelli S
Universita degli Studi, Rome, Italy
Tumori; 67(2,SupplA):102 1981

The presence of receptors for glucocorticoids (GCR) in leukemia cells does not represent a condition sufficient to warrant the response to glucocorticoids. Functional alterations in the receptor mechanism may cause corticoresistance in the cells despite the presence of appreciable receptor levels making glucocorticoids useless in polychemotherapy schemes. In order to evaluate the effectiveness of the receptor system in vitro, we measured GCR levels and the ability of glucocorticoids to induce glutamine synthetase (EC 6.3.1.2; GS) activity in the lymphoblasts of 15 patients with acute lymphatic leukemia (ALL). The results show that GS is specifically induced by glucocorticoids as previously observed in other target tissues of these steroids. Besides there is a significant correlation (r equals 0.67; p less than 0.01) between the number of receptor sites per cell and GS inducibility. This correlation seems even more significant r equals 0.83; p less than 0.001) if GCR are replaced by the binding effectiveness of receptor sites (BE),

suggesting that in addition to their numbers, receptor site affinity is also an important parameter in evaluating functional activity. In the lymphoblasts of 4 of the 15 cases examined there was no GS induction by glucocorticoids; the failure to induce was related to neither the number of GCR/cell nor the BE, suggesting the presence of defects in the receptor mechanism distal to the receptor-hormone reaction. In conclusion, our results suggest that GS inducibility by glucocorticoids may be a valid marker of GCR function in the lymphoblasts of ALL (no Refs) (In ITA)

### 70. THE SPONTANEOUS AND INDUCED SYNTHESIS OF EPSTEIN-BARR VIRUS ANTIGENS IN RAJI CELLS IMMOBILIZED ON SURFACES COATED WITH ANTI-LYMPHOCYTE GLOBULIN.

**Baylis GJ, Wolf H**
**Max von Pettenkofer Inst., Pettenkoferstrasse 9a, 8000 Munich 2, W. Germany**
**J Gen Virol; 54(part2):397-401 1981**

Immobilization of Raji cells on surfaces coated with anti-lymphocyte globulin (ALG) at low densities lead to the synthesis of Epstein-Barr virus (EBV) early antigen (EA) in up to 5% of the cells. At higher cell densities the percentage of antigen-positive cells decreased and at confluency no antigen synthesis was observed. Addition of iododeoxyuridine (IdUrd) to low density cultures increased the expression of EA to 20%, whereas in confluent cultures the cells could not be induced to synthesize EA. Treatment of cells in suspension with ALG failed to induce EA synthesis and did not potentiate the effect of IdUrd. Immobilized Raji cells proved to be suitable targets for superinfection with EBV derived from P3HR1 cultures. (Author abstract) (11 Refs)

### 71. DISTRIBUTION AND MOVEMENT OF CONCANAVALIN A RECEPTORS ON A SURFACE OF SUSPENDED CELLS.

**Domnina LV, Pletiushkina OIu**
**Res. Interfaculty Lab. Molecular Biology and Bioorganic Chemistry, State Univ., Moscow, USSR**
**Tsitologiia; 23(6):615-619 1981**

Distribution and movement of surface concanavalin A (Con A) receptors was studied in a suspension of normal murine fibroblasts, transformed murine fibroblasts L, ascites hepatoma 22 cells, ascites Krebs II cells, and murine spleen lymphocytes. Incubation of all cell types tested with Con A induced formation of receptor patches. Capping was observed only in suspension of spleen lymphocytes. (12 Refs) (In RUS)

### 72. MURINE T CELLS THAT LYSE ANTIBODY-SENSITIZED TARGET CELLS. III. CONTRIBUTION OF THY 1-BEARING CELLS TO THE LYTIC ACTIVITY OF NORMAL SPLEEN.

**Lamon EW, Pollok BA, Walia AS, Fuson EW, Williams B**
**Univ. Alabama in Birmingham, Dept. Surgery and Microbiology, Birmingham Veterans Admin. Hosp., University Station, AL, 35294**
**Immunology; 43(4):643-651 1981**

Murine spleen cells were analyzed for their capacity to lyse 51Cr-labeled antibody-sensitized RBC and a human lymphoma cell line. Incubation of spleen cells with iron powder followed by removal of iron-containing cells with a magnet significantly decreased the lytic capacity of the remaining cells against RBC target cells. However, substantial cytotoxicity remained in the relatively phagocyte-depleted population. Both antibody-sensitized RBC and tumor cells were lysed by phagocyte-depleted effector cells. However, more spleen cells were required to lyse nucleated target cells than were required to produce comparable lysis of the RBC. Such phagocyte-depleted spleen cells were subsequently treated with three different antisera containing specificities for thymus-dependent antigens and a monoclonal IgM anti-Thy 1.2 in the presence of complement. The remaining viable cells were recovered and tested as effector cells. All four reagents in the presence of complement caused an inhibition of antibody-dependent cell-mediated cytotoxicity (ADCC) that was proportional to the percentage of T cells eliminated. However, the antisera also inhibited ADCC in the absence of complement, even when the cells were trypsinized following the antiserum treatment to remove attached antibodies. On the other hand, treatment of spleen cells with the monoclonal IgM anti-Thy 1.2 followed by trypsin treatment did not inhibit ADCC unless complement was added. Thus, with the latter reagent, decreased ADCC could be ascribed to elimination of T cells and not immune complex inhibition. Cells bearing Thy 1.2 accounted for approx half of the lytic activity of phagocyte-depleted spleen cells against antibody-sensitized target cells. (Author abstract) (35 Refs)

### 73. REGULATION OF ANTIGEN-INDUCED LYMPHOPROLIFERATION BY BSA GRADIENT-SEPARATED T CELL FRACTIONS.

**Emmons RP, Carvalho EM, Horwitz DA**
**Div. Rheumatology, Dept. Internal Medicine, Univ. Virginia, Box 412, Charlottesville, VA, 22908**
**J Immunol; 127(3):821-824 1981**

Human T cells from six volunteers immunized with key-hole limpet hemocyanin (KLH) or tetanus toxoid were fractionated on bovine serum albumin (BSA) gradients. These T cell fractions were then recombined with autologous unseparated mononuclear cells or unseparated T cells to determine the effect of each fraction on the proliferative (DNA synthetic) response to the immunizing antigen. Using this separation technique, we were able to define two fractions of T cells of widely different densities that had a suppressive effect on the proliferative response to KLH of unfractionated T cells. The demonstration of suppressive activity was possible only if cells were tested within 8 wk of immunization with KLH. These suppressive T cell fractions differed not only in density but also in surface characteristics. Fraction 1 cells had a high proportion of Ia+ cells but no Fc receptors for IgG (FcRG-) were seen, whereas cells from Fraction 4 (of higher density) were Ia- and were composed of 12.1 +-1.2% FcRG+ cells. This suppression was shown to be specific for the immunizing antigen. One individual who had been immunized with KLH for more than 1 yr in which suppression of KLH-induced proliferation was no longer demonstrable was given primary immunization to tetanus toxoid. Suppression could be demonstrated in Fractions 1 and 4 specific for tetanus toxoid; there was no demonstrable effect of these T cell fractions on the response to KLH. We postulate that these are different functional populations of suppressor T cells that regulate antigen specific lymphoproliferation. (Author abstract) (26 Refs)

## OTHER RELATED STUDIES

### 74. TRANSPLANTATION FOR ACUTE LEUKAEMIA WITH HLA-A AND B NONIDENTICAL PARENTAL MARROW CELLS FRACTIONATED WITH SOYBEAN AGGLUTININ AND SHEEP RED BLOOD CELLS.

Reisner Y, Kirkpatrick D, Dupont B, Kapoor N, Pollack MS, Good RA, O'Reilly RJ
Memorial Sloan-Kettering Cancer Center, Box 380, 1275 York Ave., New York, NY, 10021
Lancet; 2(8242):327-331 1981

A new procedure for enrichment of marrow precursors and removal of T lymphocytes from large vol of human bone marrow, involving initial differential agglutination of T lymphocytes and mature marrow elements with soybean agglutinin, followed by rosetting with sheep RBCs, was used to fractionate marrow cells from an HLA-A, B, DR non-identical, MLC non-reactive, paternal donor for transplantation into an infant with acute leukemia. This transplant became completely engrafted and resulted in full recovery of normal, donor-derived hematopoietic function without graft-versus-host disease, sustained for 11 wk after transplantation, at which time the patient's leukemia recurred. Subsequently, the patient received chemotherapy and achieved a remission with regeneration of normal marrow cells of donor origin. The patient's course demonstrated the potential of lectin-separated marrow grafts to restore durable hematopoiesis, without graft-versus-host disease, in a lethally irradiated allogeneic host. (Author abstract) (23 Refs)

### 75. COMMON NEUROECTODERMAL ANTIGENS ON HUMAN MELANOMA, NEUROBLASTOMA, RETINOBLASTOMA, GLIOBLASTOMA AND FETAL BRAIN REVEALED BY HYBRIDOMA ANTIBODIES RAISED AGAINST MELANOMA CELLS.

Liso SK, Clarke BJ, Kwong PC, Brickenden A, Gallie BL, Dent PB
McMas. Univ., Health Sciences Centre, 1200 Main St., West, Hamilton, Ontario, L8N 3Z5, Canada
Eur J Immunol; 11(6):450-454 1981

The hybridoma system has been utilized to produce antibodies to characterize the cell surface antigens on human melanoma cells. On initial screening, two antibodies derived by the fusion of mouse myeloma cells (SP2/O-Ag14) and splenocytes from a mouse immunized with a melanoma cell line (CaCl 78-1) showed cross-reactivity with 10 melanoma cell lines and did not react with any of 4 epithelial cancer lines, or 4 normal adult fibroblast lines. However, because of reactivity with two neuroblastoma cell lines, additional testing with other neuroectodermal derivatives was carried out and revealed a broad cross-reactivity among melanomas, neuroblastomas, retinoblastomas and glioblastomas and against antigen s shared by fetal but not adult brain. Thus, these results indicate the existence of common neuroectodermal antigens on melanoma cells. Before melanoma specificity can be claimed for, an antibody reactivity with nonmelanoma cells bearing these neuroectodermal antigens should be excluded. (Author abstract) (21 Refs)

### 76. BIOLOGIC DIFFERENCES BETWEEN NEUROBLASTOMA STAGES IV-S AND IV. MEASUREMENT OF SERUM FERRITIN AND E-ROSETTE INHIBITION IN 30 CHILDREN.

Hann HL, Evans AE, Cohen IJ, Leitmeyer JE
Inst. Cancer Res., Fox Chase Cancer Center, 7701 Burholme Ave., Philadelphia, PA, 19111
N Engl J Med; 305(8):425-429 1981

Seventeen patients (2 mo-4 yr old) with Stage IV neuroblastoma treated with vincristine, cyclophosphamide, and imidazole carboxamide, and 13 patients (1-10 mo old) with Stage IV-S disease who were untreated were investigated for serum ferritin and erythrocyte (E)-rosette inhibition. Fifteen of the 17 patients with Stage IV neuroblastoma had positive tests for serum ferritin determined by counterelectrophoresis (CEP); all 13 patients with Stage IV-S disease were negative. When levels were tested using radioimmunoassay (RIA), only 4/15 Stage IV patients who had positive tests by CEP had ferritin levels above 400 nanog/ml, and 11 had levels between 128 and 376 nanog/ml. RIA revealed ferritin levels between 7.1 and 106 nanog/ml in the 13 Stage IV-S patients. Of the 17 Stage IV patients, 12 had E-rosette inhibition of more than 15% and all 12 had increased serum ferritin by CEP. Of the five Stage IV patients with less than 15% inhibition, three had elevated serum ferritin. Of the 13 Stage IV-S patients, only one had E-rosette inhibition above 15%. These results suggest that Stages IV and IV-S neuroblastoma can be differentiated by serum ferritin determinations by CEP and by lymphocyte E-rosette inhibition. (26 Refs)

### 77. MONOCLONAL ANTIBODY TO A NOVEL LYMPHOCYTE FUNCTION-ASSOCIATED ANTIGEN (LFA-1): MECHANISM OF BLOCKADE OF T LYMPHOCYTE-MEDIATED KILLING AND EFFECTS ON OTHER T AND B LYMPHOCYTE FUNCTIONS.

Davignon D, Martz E, Reynolds T, Kurzinger K, Springer TA
Lab. Membrane Immunochemistry, Sidney Farber Cancer Inst., Harvard Medical Sch., Boston, MA, 02115
J Immunol; 127(2):590-595 1981

The M7/14 monoclonal antibody (MAb) has previously been shown to block xenogeneic cytolytic T lymphocyte-(CTL) mediated killing by binding to the CTL rather than the target cell. It defines a novel surface antigen, termed LFA-1, with polypeptide chains of 180,000 and 95,000 Mr. The mechanism of this blockade and the effects of M7/14 on other T and B lymphocyte functional responses have been investigated here. Blockade of CTL-mediated killing is given by purified M7/14 MAb, and is not due to trivial mechanisms such as toxicity or agglutination. M7/14 blocks CTL directed to allogeneic and a nti-modified self as well as xenogeneic determinants. Blockade occurs at the recognition-adhesion step, as shown by inhibition of CTL-target cell conjugate formation. M7/14 antibody was also shown to block a variety of other T cell functions: the mixed lymphocyte response (both in xenogeneic and allogeneic systems), antigen-specific T cell proliferation, and T cell-dependent plaque-forming cell responses, but not T cell-independent plaque-forming cell responses or LPS-induced B cell proliferation. Inhibition of both CTL and MLR function was extremely potent, occurring at MAb concentrations as low as 0.5 ug/ml. Inhibition of the MLR occurs in the 1st day of 6-day cultures. The data suggest that LFA-1 participates in or is closely associated with a number of different T lymphocyte functional pathways. LFA-1 appears crucial for the adhesive interaction between CTL and target cells, and it is possible that its importance in T helper and proliferative responses is

also related to intercellular interactions. (Author abstract) (33 Refs)

## 78. DETECTION AND CHARACTERIZATION OF MOUSE MAMMARY TUMOR VIRUS CELL SURFACE ANTIGENS.

Callis AH
The University of Tennessee Center, Memphis, TN
Diss Abstr Int (B); 41(12):4386-B 1981

An isotopic staphylococcal protein A test (ISPAT) employing viral-antigen specific immune sera and iodinated staphylococcal protein A (SPA) was designed to detect and quantitate mouse mammary tumor virus (MMTV) of established mammary tumor cell lines. With the ISPAT, the envelope glycoprotein, gp52, was found to be the predominant MMTV antigen detected on the cell surface of cultured mouse mammary tumor cells. A possible correlation between cell surface expression of gp52 and detection of this viral protein in the plasma of tumor-bearing animals appears likely. Dexamethasone and hydrocortisone either alone or in combination with insulin caused striking increases in the amount of gp52 detected. The ISPAT detected antigenic determinants of murine leukemia virus (MuLV) on the surface of mouse mammary tumor cells and provided relative estimates of the cell surface abundance of two sets of viral antigenic determinants (gp52 and Rauscher MuLV). This research also explored the relationship between production of MMTV, release of soluble MMTV proteins, and detecton of MMTV proteins on the cell surface of mouse mammary tumor cells. An MMTV non-producer cell line in the presence of dexamethasone could be converted into an MMTV-producing cell line by increasing its cell surface gp52 expression by only 25 per cent. Dexamethasone also resulted in an increase in cell surface expression of gp52, virus production and extracellular release of gp52 from mouse mammary tumor cells. When the extracellular gp52 was fractionated into soluble and virion-associated antigens, extracellular gp52 was predominantly detected as soluble antigen. However, virion-associated antigen wa s preferentially released upon dexamethasone stimulation. When increases in gp52 cell surface abundance were compared to increases in gp52 extracellular release following dexamethasone stimulation, increases in cell surface gp52 expression paralleled increases in extracellular gp52 release; marked differences in the magnitude of stimulation were detected. (no Refs)

## 79. STRUCTURAL CHARACTERIZATION OF HUMAN MELANOMA-ASSOCIATED ANTIGEN P97 WITH MONOCLONAL ANTIBODIES.

Brown JP, Nishiyama K, Hellstrom I, Hellstrom KE
Div. Tumor Immunology, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104
J Immunol; 127(2):539-546 1981

Monoclonal antibodies were used to study p97, a human melanoma-associated antigen (MAA). Four hybridomas, designated 4.1, 96.5, 118.1, and 8.2, were obtained by fusing mouse myeloma cells with spleen cells from mice immunized with human melanoma cells. Antibodies 4.1 and 8.2 were IgG1; antibodies 96.5 and 118.1 were IgG2a. Sequential immunoprecipitation (IP) and sodium-dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) showed that all four antibodies recognized the same 97 kilodalton (kD) protein. Binding studies with 125I-labeled antibody showed that antibodies 4.1 and 96.5 bound the same epitope, p97a. Antibodies 118.1 and 8.2 defined epitopes p97b and p97c, respectively. Six monoclonal antibodies (M17, L1, L10, R10, I12, and K5) specific for gp95, a 95 kD melanoma cell surface glycoprotein were also tested. Sequential IP showed that these antibodies bound p97; p97 and gp95 are thus identical. Binding studies showed that antibody M17 bound epitope p97a, and antibodies L1, L10, and R19 bound epitope 97c. Antibodies I12 and K5 defined two other epitopes, p97d and p97e, respectively. SDS-PAGE under on reducing conditions indicated that p97 is monomeric, probably with intrachain disulfide bonds. Cell-surface labeling of sialic acid residues and neuraminidase digestion showed that p97 is a sialoglycoprotein. Digestion of p97 with papain or trypsin produced a stable 40 kD fragment, which expressed epitopes p97a, p97b, and p97c, but not p97d or p97e. (Author abstract) (35 Refs)

## 80. STRUCTURAL PROPERTIES AND TISSUE DISTRIBUTION OF THE ANTIGEN RECOGNIZED BY THE MONOCLONAL ANTIBODY 653.40S TO HUMAN MELANOMA CELLS.

Natali PG, Imai K, Wilson BS, Bigotti A, Cavaliere R, Pellegrino MA, Ferrone S
(c/o Ferrone) Dept. Molecular Immunology, Scripps Clinic and Res. Foundation, La Jolla, CA, 92037
JNCI; 67(3):591-601 1981

The hybridoma 653.40S, constructed with splenocytes from an inbred BALB/c mouse immunized with cultured human melanoma cells, secreted an antibody that had been shown to recognize an antigenic determinant restricted to human melanoma cell lines. The monoclonal antibody (MoAb) 653.40S showed immunoprecipitation of two glycopolypeptides synthesized by melanoma cells, one with the apparent mol wt of 280,000 and the other one with a mol wt larger than 500,000. These two glycopolypeptides were not bridged by disulfide bonds and were peripheral rather than integral to the plasma cell membrane. Comparison of the reactivity of cells of the melanocyte lineage with the MoAb 653.40S and with the MoAb Q5/13 to human Ia-like antigens showed that the former reacted with proliferating melanocytes and melanoma cells, whereas the latter reacted only with melanoma cells. The MoAb 653.40S did not react with a large variety of surgically removed normal and tumor tissues except for some instances of basal cell and squamous cell carcinomas. These results suggested that double staining of pigmented skin lesions with the MoAb 653.40S and with an MoAb to Ia-like antigens may help to solve controversial diagnosis of melanoma. Furthermore, the MoAb 653.40S may be useful for radioimaging and immunotherapy of melanoma. (Author abstract) (32 Refs)

## 81. CLINICAL EVALUATION OF CARCINOEMBRYONIC ANTIGEN (CEA) LEVELS IN SERUM AND TUMOR TISSUE OF BREAST CANCER PATIENTS.

Kitamura M, Tominaga T, Kaneko H, Hayashi K, Takahashi I, Saito T, Ito I
Dept. Surgery, Tokyo Metropolitan Komagome Hosp., Tokyo, Japan
Nippon Gan Chiryo Gakkai Shi; 16(1):35-43 1981

CEA was studied in 236 patients with primary breast carcinoma, 51 with recurrent breast carcinoma, and in 14 with benign breast disease. Levels of serum CEA greater than 2.5 nanog/ml were observed preoperatively in 23/216 patients with Stage I, II, or III primary breast cancer, and postoperative increases in the levels of CEA were thought to indicate the possibility of distant metastasis. Levels of CEA greater than 2.5 nanog/ml were also observed in 11/20 patients with Stage IV primary breast cancer patients and 22/51 patients with recurrent breast cancer. Some associations were observed between the therapeutic results of particular therapies and

levels of serum CEA in 25 patients with advanced breast cancer whose levels of serum CEA were determined serially before and after treatment. Serum CEA levels were highest in patients with liver metastasis as the primary site of recurrence. Levels of CEA in tumor tissues were not related to the clinical stage of the cancers, the degree of axillary lymph nodal metastasis, histological type of the tumors, pre- or postmenopausal status of the patients, or number of estrogen receptors in the tumor tissue. All of the patients who were observed to have high levels of serum CEA also had high levels of CEA in tumor tissue, and patients with high levels of CEA in tumor tissues were thought likely to have elevated CEA levels during periods of postoperative recurrence. (16 Refs) (In JPN)

## 82. SERIAL TRANSPLANTATION OF A HUMAN T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA LINE INTO NUDE MICE.

**Miyoshi I, Ota T, Hiraki S, Sumadi M, Tanaka T, Kimura I**
**Dept. Medicine, Kochi Medical Sch., Kochi 781-51, Japan**
**Br J Cancer; 44(1):124-126 1981**

The serial transplantation of an ascites form of human T-cell acute lymphoblastic leukemia (ALL) into male and female athymic nude mice with a BALB/c genetic background is described. Of a total of 39 nude mice transplanted over a period of 15 mo, 29 showed a progressive growth of tumors, killing the hosts 29-62 days after implantation. There were multiple tumor nodules involving the intra-abdominal organs and retroperitoneums, with 0.5-6 ml of hemorrhagic ascites. Many of the tumor-bearing mice showed slight enlargement of the mediastinal lymph nodes and spleen but peripheral lymph nodes were not appreciably enlarged. Pleural effusion was also seen in a few animals. Histologically, leukemic infiltration was usually found in the liver, spleen, kidneys, lungs, and lymph nodes. In addition, a single mouse showed leukemic infiltration into the choroid of one eye. Hepatic infiltrates were diffuse in the portal and sinusoidal spaces. The ascites contained 1-4 x 10(8) tumor cells/ml. The WBC count of tumor-bearing mice was 11,000-35,000/cubic mm. Of the ascites tumor cells examined, 80-90% formed spontaneous rosettes with sheep erythrocytes. The results indicated that cells from a continuous cultures line of human T-cell ALL (TALL-1) can be serially transplanted into BALB/c nude mice. (10 Refs)

## 83. CANINE TRANSMISSIBLE VENEREAL SARCOMA: IDENTIFICATION AND FUNCTIONAL CHARACTERIZATION OF LYMPHOCYTES FROM PERIPHERAL BLOOD, DRAINING LYMPH NODES, AND TUMORS AT DIFFERENT STAGES OF GROWTH.

**Chandler JP**
**The University of Connecticut, Storrs, CT, 06268**
**Diss Abstr Int (B); 41(12):4321-B 1981**

To study the host-tumor relationship of dogs bearing the canine transmissible venereal sarcoma (CTV), lymphocytes from peripheral blood, draining lymph nodes, and tumors were monitored during the course of tumor growth and spontaneous rejection by immunofluorescence surface marker analysis, spontaneous incorporation of (3H)-thymidine, phytohemagglutinin (PHA) and protein A mitogenesis, and responsiveness to tumor-associated antigens, (TAA), CTVS cell in mixed lymphocyte tumor culture (MLTC) and allogenic lymphocytes in mixed lymphocyte reaction (MLR). Distinguishable patterns of response to CTVS were observed in dogs, depending on the growth of the tumor. It is hypothesized that the differences might be due, in part to trafficking of lymphocytes to and from the tumor. It is also suggested that results of this study illustrate the complex dynamic nature of the host-tumor relationship. (no Refs)

## 84. THETA POLYPEPTIDE PHENOTYPES OF LYMPHOID AND MYELOID CELL LINES CONTAINING RNA TRANSCRIPTS OF THE IMMUNOGLOBULIN CTHETA GENE.

**Walker ID, Harris AW**
**The Walter and Eliza Hall Inst. Medical Res., Victoria 3050, Australia**
**J Immunol; 127(2):561-566 1981**

We have examined whether polyadenylated-RNA molecules encoded by the immunoglobulin Cmu gene (Cu RNA) that have recently been shown to occur in mouse T lymphoma, myeloid tumor, and pre-B lymphoma cell lines are translated. Three T lymphoma, one myeloid tumor, and four Abelson lymphoma cell lines, all known to contain Cu RNA molecules, were examined for evidence of synthesis of mu polypeptides using radioimmunoassay, biosynthetic labeling, and immunoprecipitation techniques. No mu polypeptides were detected in any of the T lymphoma or myeloid cell lines, although mu-chains were readily detected in two B lymphoma lines known to contain small amounts of mu mRNA. Detection failure is unlikely to be the result of assay insensitivity and was not caused by lack of an appropriate antiserum reactivity or a requirement of mu-chains to be associated with immunoglobulin light chains. Proteolytic activity that might degrade newly synthesized mu polypeptides in these cell lines was not detected. In three of the four Abelson lymphoma cell lines containing Cu RNA, corresponding polypeptides were absent, although in the fourth they were easily detected, indicating that transcription of the Cu gene is not the sole determinant of whether a cell will synthesize the corresponding polypeptide. The parallel between the Cu RNA+, mu polypeptide- Abelson cell lines and the T lymphoma cell lines suggests that the onset of Cu transcription may occur in both T and B lineages before translational competence is acquired. (Author abstract) (35 Refs)

## 85. STUDIES ON NATURAL KILLER CELL AND ANTIBODY DEPENDENT CELL MEDIATED CYTOTOXICITY IN GNOTOBIOTIC AND CONVENTIONAL C3H/HECR MICE.

**Schmitz HE**
**University of Notre Dame, Notre Dame, IN**
**Diss Abstr Int (B); 41(11):4061-B 1981**

Normal and Poly I:C stimulated levels of murine NK and ADCC activities were measured using a short term in vitro 51Cr release assay in which spleen cells prepared from both germfree and conventional C3H/HeCr inbred mice were used as a source of effector cells and YAC-1 Moloney virus induced leukemic cells, RL 1 radiation induced by lymphoma cells, and nucleated chicken RBC were used as target cells. For proper statistical analysis, the mice were sacrificed according to two experimental designs at 6, 12, 16, 24, and 42 wk of age. The results of this study indicated that the presence of a viable murine microflora is not required for the age-dependent expression of either NK or ADCC activity, that the presence of such a microflora modulates both the normal and potential level of NK and ADCC activity expressed by conventional mice, and that the absence of such a microflora alters the quantitative but not qualitative expression of NK and ADCC cytotoxicities in the experimental mouse strain. Additional characterization studies indicated tha t the spleen cell population re-

sponsible for the observed ADCC activities consisted of nonadherent nonphagocytic, Ig cells that could also express low levels of Thy-1 surface determinants. The effector cells responsible for the observed NK activities were found to be nonadherent, nonphagocytic, Ig cells that would express Thy-1 membrane determinants when stimulated in vivo with Poly I:C. Together, the results of this study suggest that germfree inbred mice can be used as controlled model systems for the study of the biological implications of NK and ADCC cytotoxicities. (no Refs)

## 86. NATURAL KILLER CELL ACTIVITY IN A POPULATION OF LEUKEMIA-PRONE WILD MICE (MUS MUSCULUS).

**Scott JL, Pal BK, Rasheed S, Gardner MB**
**(c/o Gardner) Dept. Pathology, Univ. California Sch. Medicine, Davis, CA, 95616**
**Int J Cancer; 28(2):241-247 1981**

Natural cell-mediated cytotoxicity against YAC-1 targets was measured in splenocytes from leukemia-prone wild mice trapped near Lake Casitas (LC) in southern California. Cytotoxicity was mediated by cells that were non-adherent to nylon wool, non-phagocytic and resistant to thy-1.2 antiserum plus complement. Natural MuLV viremia in LC mice did not impair splenic cytotoxicity against YAC-1 target cells. Cells infected with amphotropic and ecotropic MuLV of wild mouse origin were not appreciably lysed by LC splenic effectors. Although variable levels of cytotoxicity were detected against YAC-1 by normal LC spleen cells, consistently low levels of cytotoxicity against allogenic LC lymphoma, sarcoma and carcinoma targets were found using the same splenocytes. These results indicate that LC mice possess splenocytes with the characteristics of natural killer (NK) cells as defined in inbred mice. The resistance of LC-derived targets to lysis by LC NK cells suggests that NK cells may not be involved in natural tumor immunosurveillance or that the development of spontaneous tumors may involve escape from NK-mediated effector mechanisms. (Author abstract) (46 Refs)

## 87. THE DETECTION OF EPSTEIN-BARR VIRUS RECEPTORS UTILIZING RADIOLABELLED VIRUS.

**Koide N, Wells A, Volsky DJ, Shapiro IM, Klein G**
**Dept. Internal Medicine, Okayama Univ. Sch. Medicine, 5-1, 2-chome, Okayama 700, Japan**
**J Gen Virol; 54(part1):191-195 1981**

Epstein-Barr virus (EBV) was labeled with 3H-thymidine and purified about 1000-fold from the culture medium by ultracentrifugation on 5 to 30% dextran gradients. The presence of the virus was monitored by radioactivity and Epstein-Barr virus-determined nuclear antigen (EBNA) induction in sensitive indicator cells (Ramos). Peaks for both activities occurred in the 17 to 18% dextran fractions. Unlabeled virus recovered in the peak fraction was labeled with 125I. Both thymidine and 125I-labeled purified virus bound quantitatively to receptor-positive Burkitt lymphoma-derived cell lines but not to EBV-receptor -negative T-lymphocyte-derived cell lines. Thymidine-labeled virus that was allowed to bind to Raji cells was present in the interior of briefly trypsinized cells after 3 hr incubation at 37 C. The results provide a convenient method for detecting the EBV receptor by radioactively labeled virus. (Author abstract) (15 Refs)

# AUTHOR INDEX WITH CITATION NUMBERS


Agostini C. 34
Aikawa K. 6
Andreewa P. 1
Aoki T. 62
Asofsky R. 20
Aubry J. 21
Ballas ZK. 48
Baltimore D. 22
Bayle C. 18
Baylis GJ. 70
Bazin H. 33
Bernard A. 11
Bernard A. 18
Bezou MJ. 11
Bier J. 63
Bigotti A. 80
Bluestone JA. 37
Bollum FJ. 62
Boltz-Nitulescu. 33
Bono R. 44
Bosma MJ. 29
Bosma MJ. 30
Boss MA. 22
Bottura C. 36
Boumsell L. 11
Boumsell L. 18
Bray J. 17
Brickenden A. 75
Britt WJ. 51
Brown JP. 79
Buchanan PD. 32
Burns GF. 2
Cacciola E. 35
Calkins CE. 47
Callis AH. 78
Carpentieri U. 67
Carvalho EM. 73
Cavaliere R. 80
Ceriani RL. 19
Chandler JP. 83
Chandler P. 50
Chesebro B. 51
Clarke BJ. 75
Cohen IJ. 76
Coombes RC. 15
Coppin H. 18
Dan S. 62
Darfler FJ. 60
Davies AJ. 7
Davignon D. 13
Davignon D. 25
Davignon D. 77
De Rossi G. 3
DeLeo AB. 26
DeRossi G. 69
Dearnaley DP. 15
Delia D. 14
Demeocq F. 11
Dent PB. 75
Domnina LV. 71
Dreyfuss G. 22
Dunlop N. 52
Dupont B. 74
Edwards SA. 42
Emmons RP. 73
Evans AE. 76
Falcao RP. 36
Fan H. 42
Fast LD. 38
Fellous M. 44
Ferguson RM. 65
Fernandes G. 12
Ferrone F. 57
Ferrone S. 80
Fischinger P. 52
Fleissner E. 26
Frank M. 55
Freeman C. 54
Freeman C. 55
Fuller CR. 32
Fuson EW. 72
Gadek J. 55
Gallie BL. 75
Gardner FH. 67
Gardner MB. 86
Gasparotto G. 34
Germain RN. 13
Gidlund M. 31
Gifford RR. 65
Giustolisi R. 35
Glassy MC. 57
Goding JW. 2
Good RA. 74
Gooding LR. 49
Grant CK. 27
Greaves M. 14
Green WR. 48
Gresser I. 44
Guglielmo P. 35
Gugliemi C. 3
Gupta S. 12
Gustafsson A. 41
Habeshaw JA. 7
Hachiya T. 9
Hammerling U. 24
Hammerling U. 26
Hammerling Y. 46
Hann HL. 76
Hansen JA. 38
Hansen JA. 5
Hanto DW. 39
Harris AW. 84
Hayashi K. 81
Hellstrom I. 79
Hellstrom KE. 79
Hemmerling U. 56
Henney CS. 48
Hersey P. 4
Hiraki S. 82
Hood P. 10
Horwitz DA. 73
Hughes RJ. 60
Huhn D. 1
Hurtenbach U. 37
Hyafil F. 44
Iacobelli S. 69
Ihle J. 52
Imai K. 57
Imai K. 80
Ingenito GG. 47
Insel PA. 60
Ishii Y. 6
Ito I. 81
Jansson M. 31
Kabat D. 23
Kadin ME. 5
Kagan E. 61
Kamoun M. 5
Kaneko H. 81
Kapoor N. 74
Kemshead J. 14
Kennedy R. 7
Kikuchi K. 6
Kim JK. 20
Kimura I. 82
Kimura S. 24
Kimura S. 46
Kirch ME. 56
Kirkpatrick D. 74
Kitamura M. 81
Klein G. 64
Klein G. 87
Koide N. 87
Kuppers RC. 48
Kurzinger K. 13
Kurzinger K. 25
Kurzinger K. 77
Kwong PC. 75
Lamon EW. 72
Laskov R. 20
Lazar A. 40
Leitmeyer JE. 76
Liao SK. 75
Liu Y. 24
Liu Y. 46
Longo P. 69
Lopez C. 37
Lopez M. 3
Lundgren E. 41
Lutz H. 28
Machida C. 23
Magrath I. 54
Magrath I. 55
Malpuech G. 11
Mandelli F. 3
Marchetti P. 69
Marta E. 77
Martin PJ. 5
Martz E. 13
Martz E. 25
McKeever PE. 20
McKolanis JR. 66
McPherson TA. 17
Michalek MT. 27
Mikuni C. 6
Minai M. 40
Minato K. 9
Minguell JJ. 67

Miyoshi I. 82
Mizrahi A. 40
Najarian JS. 39
Nakamura H. 43
Natali PG. 80
Natoli V. 69
Nettleton J. 5
Newman R. 14
Newman W. 38
Ng AK. 57
Nicklisch U. 63
Nilsson K. 31
Nishiyama K. 79
Novikovs L. 54
Novikovs L. 55
O'Donnell PV. 26
O'Donnell PV. 58
O'Reilly RJ. 74
Obata Y. 58
Oettgen HF. 53
Ogasawara M. 6
Old LJ. 58
Ora A. 31
Ota T. 82
Pal BK. 86
Paraf A. 21
Pasqualetti D. 3
Pattengale PK. 31
Pellegrino MA. 80
Peterson JA. 19
Pezzutto A. 34
Pham D. 18
Pierotti M. 26
Pinter A. 26
Pletiushkina OI. 71
Pole D. 50
Pollack MS. 74
Pollok BA. 72
Pommier P. 21
Potter M. 21
Prensky W. 28
Pullen S. 4
Purtilo DT. 39
Raimondi R. 34
Ranelletti FO. 69
Rasheed S. 86
Raynal B. 18
Reisner Y. 74
Reuveny S. 40
Reynolds T. 13
Reynolds T. 25
Reynolds T. 77
Richard Y. 18
Rippey JH. 10
Rizzo M. 35
Rodt H. 1
Rose ML. 7
Rosenthal KS. 59
Ruscetti S. 28
Saito T. 62
Saito T. 81
Sakamoto K. 39
Santaella M. 55
Sasaki R. 62
Schmitz HE. 85
Schneider C. 14
Scott JL. 86
Semenzato G. 34
Shapiro IM. 64
Shapiro IM. 87
Shimoyama M. 9
Shuman H. 59
Simmons JG. 32
Simmons RL. 39
Simonin G. 21
Simpson E. 50
Singh SN. 21
Sloane J. 7
Smith LJ. 16
Snodgrass HR. 29
Snodgrass HR. 30
Spiegel R. 55
Spiegelberg HL. 33
Springer TA. 13
Springer TA. 25
Springer TA. 77
Stockert E. 58
Strominger JL. 59
Sumadi M. 82
Sun T. 8
Sutherland R. 14
Tada N. 24
Tada N. 46
Takahashi I. 81
Takaku F. 62
Tanaka T. 82
Taylor BA. 46
Thiel E. 1
Thiel H. 52
Tominaga T. 81
Traub A. 40
Turchini MF. 11
Urivetzky M. 68
Varsano-Aharon. 68
VedBrat SS. 28
Viadro MM. 45
Volsky DJ. 64
Volsky DJ. 87
Voss BV. 65
Walia AS. 72
Walker ID. 84
Watanabe S. 9
Wells A. 87
Whitmore AC. 49
Wigzell H. 31
Williams B. 72
Wilson BS. 80
Wilson DB. 29
Wilson DB. 30
Wiltshaw E. 7
Wolf H. 70
Wood WG. 10
Woods VL. 20
Yamashita U. 43
Yount WJ. 32
Zachowski A. 21

# More Than Just A Fancy Name

**Mention CANCERLINE to your librarian** and the world's foremost collection of cancer information is at your disposal. With the help of this computerized data system, you can obtain information on the following:

## Cancer Literature

The literature date base, **CANCERLIT**, allows you to survey more than 3,000 biomedical journals for information on your topic of interest. Your search will also alert you to meeting proceedings, monographs, and books published in that area. Informative abstracts averaging 200 words are provided with each citation;

## Current Cancer Research

The data base **CANCERPROJ** allows you to retrieve descriptions of current work in any cancer research area. The descriptions, which state research objective, methodology, and experimental results, are supplied for projects underway in 77 countries around the world.

## Cancer Therapy Protocols

The **CLINPROT** section of CANCERLINE is designed primarily for clinicians. It provides detailed summaries of currently active experimental protocols for any cancer site, agent, or type.

**Ask your biomedical librarian about CANCERLINE.**
CANCERLINE is sponsored by the International Cancer Research Data Bank—a program of the National Cancer Institute.

CANCERLINE

# Keep Up with the Cancer Literature

## Each Month
## You Can Receive Abstracts
## Covering Your Specialty Area

- This convenient service — called Auto SDI* — is as near as your nearest biomedical library. Discuss your research interests with the librarian who will design an appropriate search strategy.
- Abstracts of the latest published literature are searched automatically each month and those related to your interests are delivered to you on a regular basis.
- The abstracts you receive are selected from more than 4,000 monthly entries made into CANCERLIT — the extensive cancer literature data base of the National Cancer Institute.

## Talk With Your Librarian
## About the Auto SDI Service TODAY.

*Auto SDI stands for Automatic Selective Dissemination of Information. It is a service provided to you, at minimal cost, by the International Cancer Research Data Bank (ICRDB) — a part of the National Cancer Institute.

**U.S. DEPARTMENT OF COMMERCE**
**National Technical Information Service**
5285 Port Royal Road
Springfield, Va. 22161

OFFICIAL BUSINESS

Penalty for Private Use, $300

**PRINTED MATTER**

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF COMMERCE
COM-211

THIRD CLASS
BULK RATE

U.S.MAIL

CB-17

**CANCERGRAMS are distributed for the International Cancer Research Data Bank (ICRDB) by the National Technical Information Service (NTIS). CANCERGRAMS are available from NTIS on a standing order basis at $2 each for North American Continent addressees and $3 each for other addressees. An NTIS deposit account is required. For a list of subject categories or other information, please write to:**

**Subscription Section**
**National Technical Information Service**
**5285 Port Royal Road**
**Springfield, VA 22161**

**NOTICE OF MAILING CHANGE**

☐ Check here if you wish to discontinue receiving this publication.

☐ Check here if your address has changed and you wish to continue receiving this publication. (Be sure to furnish your complete address including zip code.)

Tear off cover with address label still affixed and send to:

Computer Support Center
ICRDB Program
IIT Research Institute
10 West 35th Street
Chicago IL. 60616

CB 17/82/02

NCI/ICRDB/CB17 82/02

PB82 931802

# ICRDB CANCERGRAM

# IMMUNOBIOLOGY AND CANCER

## Identification and Characterization of Immune Cells

SERIES CB17 No. 82/02

FEBRUARY, 1982

This Cancergram is a service of the INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM of the U.S. National Cancer Institute. Every few weeks, an updated Cancergram containing abstracts of selected cancer-related articles recently published in more than 3000 journals, and dealing with the topic indicated by the above title, is sent to researchers working in this area. These researchers are identified on the basis of the description of their current research project that has been submitted to the ICRDB Program, directly or via granting agencies.

This Cancergram is prepared by the Cancer Information Dissemination and Analysis Center (CIDAC) for Virology, Immunology, and Biology. ***If this Cancergram is useful and valuable, please send your comments to the CIDAC address below, since future editions depend on user satisfaction and user needs:***

CIDAC FOR VIROLOGY, IMMUNOLOGY, AND BIOLOGY
SCIENCE INFORMATION SERVICES
FRANKLIN INSTITUTE RESEARCH LABORATORIES
20TH AND RACE STREETS
PHILADELPHIA, PA 19103

NEWARK PUBLIC LIBRARY

APR 15 1982

U. S. GOVT. PUBS.
DEPOSITORY 376

VISIT THE ICRDB BOOTH DURING THE ASCO/AACR MEETINGS FOR COMPLEMENTARY SEARCHES OF CANCERLINE IN ADDITION TO SAMPLE COPIES OF ICRDB PUBLICATIONS.

*In this issue:*


- **CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS..... 1-12**
- **DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS..... 13-21**
- **LYMPHOCYTE AND DIFFERENTIATION ANTIGENS..... 22-27**
- **CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION..... 28-30**
- **EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS..... 31-37**
- **OTHER RELATED STUDIES..... 38-50**


**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Public Health Service • National Institutes of Health • National Cancer Institute**

HE 20.3173/2:

## CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS

### 1. LOW- AND HIGH-RISK NON-T NON-B AND T-CELL ACUTE LYMPHOID LEUKEMIA (ALL) IN CHILDHOOD: DIFFERENT DURATION OF REMISSION AND SURVIVAL.

Imbach P, Baumgartner C, Berchtold W, Gautier E, Gugler E, Hirt A, Morell A, Tonz O, Wyss M, Zurbrugg R, Wagner HP
Universitatskinderklinik Inselspital, CH-3010, Bern, Switzerland
Med Pediatr Oncol; 9(4):309-317 1981

In a prospective, nonrandomized trial clinical (initial WBC and chest film) and immunological (surface immunoglobulin and rosetting with pretreated sheep SRBC) criteria were used to s tratify 69 children with previously untreated acute lymphoid leukemia (ALL). Forty of 61 evaluable patients had low risk (ALL) (initial WBC 20,000/mm3 or less, no mediastinal mass) and were treated less intensively. Twenty-one of 61 patients had high-risk ALL (initial WBC greater than 20,000/mm3 and/or mediastinal mass) and were treated more intensivy. Of the high-risk patients 15 had non-T non-B and 6 T ALL. Sixty of 61 patients went into complete remission. After a median observation period of 27 mo, 32 of 40 low-risk, 7 of 14 high-risk non-T non-B, and none of 6 high-risk T ALL patients were in continuous first remission. Thirty-six of 40 low-risk, 9 of 15 high-risk non-T non-B, and none of 6 T ALL patients were alive. Despite more intensive treatment, the duration of remission and the survival were significantly shorter in the high-risk than in the low-risk patients. Among the high-risk ALL, non-T non-B ALL did better than T ALL. (Author abstract) (33 Refs)

### 2. PROGNOSTIC SIGNIFICANCE OF THE T-CELL-MARKER IN CHILDHOOD ACUTE LYMPHATIC LEUKEMIA.

Pluss HJ, Joller PW, Hitzig WH
Univ.-Kinderklinik, Steinwiesstrasse 75, CH-8032 Zurich, Switzerland
Schweiz Med Wochenschr; 111(41):1527-1531 1981

Of 58 children with acute lymphatic leukemia who had undergone marker studies of blasts, only 6 (10%) had greater than 30 E+ blasts. Of these, five had a high WBC and organomegaly, but only two suffered a fatal course. Two more have been in CCR for over 5 yr despite other risk factors. Patients with less than 30% E+ cells did not differ from common ALL patients clinically or in their response to treatment. However, three older children with Hp-positive but E negative blasts had a very high WBC and died without having remission. Only standardized marker studies, treatment and follow-up of a large series of ALL patients will show the importance to be attached to these and other T-cell markers compared with the better-known clinical and hematologic risk factors. (Author abstract) (3 Refs) (In GER)

### 3. THE DIAGNOSTIC SIGNIFICANCE OF T- AND B-ROSETTE FORMATION AND NON-SPECIFIC ACID ESTERASE IN THE DIFFERENTIAL DIAGNOSIS OF ACUTE AND CHRONIC LEUKEMIA.

Gudat F, Albrecht R, Kasper M, Krey G, Durmuller U, Heitz Ph, Ludwig Ch, Christen Ch, Obrecht JP
Institut fur Pathologie der Universitat, Schonbeinstrasse 40, CH-4056 Basel, Switzerland
Schweiz Med Wochenschr; 111(36):1325-1330 1981

The diagnostic significance of acid non-specific alpha-naphthyl-acetate esterase (ANAE) and of rosette formation of leukemic cells with sheep and mouse RBC was studied in 8 patients with acute myeloid leukemia (AML), in 4 patients with acute lymphatic leukemia (ALL) and in 14 patients with chronic lymphatic leukemia (CLL). ANAE showed typical diffuse cytoplasmic activity in all cases of AML. The enzyme activity was granular in both of the lymphoid malignancies, T-ALL and B-CLL, allowing differentiation from AML but not between B- and T-leukemia cells. Rosette formation with mouse RBC (ME) was diagnostic in all 14 cases of CLL and superior to labeling of surface Ig (8 of 14 cases positive). ME-rosette forming myeloblasts were detected in two of four evaluated cases of AML. Rosette formation with sheep RBC (SE), including cytological evaluation of rosette-forming cells, was diagnostic in all cases of ALL (= T-ALL). In six of nine patients with AML, however, rosette formation with SE was observed in a few cells, including myeloblasts with Auer rods. The occurrence of blasts in myeloid leukemia carrying lymphoid cell markers is discussed in the light of recent findings, according to which lymphoblastoid cells may arise in the course of myeloid leukemia requiring antileukemic treatment different from that of AML. (Author abstract) (18 Refs) (In GER)

### 4. SCANNING IMMUNO-ELECTRON MICROSCOPY OF HUMAN LEUKAEMIA AND LYMPHOMA CELLS: A COMPARATIVE STUDY OF TECHNIQUES USING IMMUNOLATEX SPHERES AS MARKERS.

Gamliel H, Leizerowitz R, Gurfel D, Polliack A
Dept. Hematology, Hadassah Univ. Hosp., Jerusalem, Isreal
J Microsc; 123(2):189-199 1981

Scanning immuno-electron microscopic (SIEM) techniques were used to identify human leukemia-lymphoma cells, using monodispersed polystyrene (latex) beads conjugated to specific antisera by glutaraldehyde (immunolatex spheres). A variety of cells of known origin were studied in an attempt to detect surface antigenic components. The antisera were usually immunoglobulin fractions and were prepared against human thymus-derived (T) cells, common type acute lymphoblastic leukemia (C/ALL) cells, and surface immunoglobulin (sIgG)-bearing cells. Several types of experiments were carried out: (1) to determine whether it is essential to neutralize fixed samples with glycine before the addition of immunolatex, (2) to test the immunospecificity of the antisera conjugated to the latex spheres, using both fixed and unfixed cells, and (3) to ascertain the surface morphology of human leukemia-lymphoma cells positively labeled with the specific antisera. Glycine treatment was essential for detecting specific antigenic sites on the cell surface by SIEM. The immunospecificity of the heteroantisera was adequate; insignificant non-specific attachment and cross reactivity were seen. SIEM is a useful technique for ultrastructural studies of the human leukemia-lymphoma cells and is a potentially useful tool in their identification. (32 Refs)

## 5. A NEW LOOK AT MALIGNANT LYMPHOMAS.

Parker JW
Sch. Medicine, Univ. Southern California, Los Angeles, CA
Diagn Med; 4(4):77-80,85,87-90,92,94,96,98-100,103-105,108,110,113 1981

A general review is presented of malignant lymphomas (ML), the diagnosis and tre atment of which has greatly improved in the last 10 yr. The classification of ML as either lymphocytic or histiocytic is being reconsidered today in light of our new understanding that the immune system consists of three major compartments: T and B lymphocytes, and histiocytes/macrophages and that malignant cells can arise from any of these compartments. The process and results of lymphocyte transformation in vitro have been studied extensively. B cell lymphomas develop as transformations in the follicular centers of lymphoid tissues. The genesis of T cell lymphomas is less well understood. Both T and B cells have immunoregulatory functions that may be retained by neoplastic lymphoid cells. Many immunological, functional, and cytochemical markers are useful for distinguishing T cells, B cells, and histiocytes; combinations of these markers also distinguish lymphoma/leukemia cells. Cytochemical and histochemical procedures can be used to identify leukemias and lymphomas, although no one stain or enzyme is totally specific for a given neoplastic cell type. Immunohistochemistry and immunocytochemistry have become useful in diagnosis, particularly techniques using antibodies conjugated with enzymes. The application of these methods and concepts to the differentiation of lymphomas and leukemias is discussed. Lymphocytic lymphomas are neoplasms of the immune system that may represent cells that are blocked in certain stages of their normal development or transformation. (22 Refs)

## 6. CYTOGENETIC FINDINGS IN T-ZONE LYMPHOMA.

Godde-Salz E, Schwarze EW, Stein H, Lennert K, Grote W
Dept. Human Genetics, Univ. Kiel, Schwanenweg, D-2300 Kiel, W. Germany
J Cancer Res Clin Oncol; 101(1):81-89 1981

Histologic, immunologic, and cytogenetic findings are reported for five non-Hodgkin's lymphomas that fulfilled the diagnostic criteria of T-zone lymphoma; ie, they contained all the T-region components of lymphoid tissue and also B-region remnants. The patients, aged 64-77 yr, included two women and three men. In 4/5 cases, the lymph node architecture was completely effaced, with the exception of the residual B areas (follicles). The B cells were identified immunologically as the nonneoplastic cells, and the cells that formed rosettes with sheep RBC were found to be the tumor cells. The chromosome analyses revealed abnormal clones as well as normal mitoses in four cases. Structural rearrangements involved chromosomes 1, 2, 3, 4, 14, and Y. Some tumors showed the loss of chromosomes 3, 5, 6, or 13 and some a gain of chromosomes 3 and 9. There was a high frequency of structural and numerical aberrations in chromosome 3, but a low frequency of 14q markers in one case. The number of patients was too small to determine whether this pattern is specific for the T-zone lymphomas. (21 Refs)

## 7. T GAMMA CELLS: A MISSING LINK BETWEEN MALIGNANT HISTIOCYTOSIS AND T CELL LEUKEMI A-LYMPHOMA?

Kadin ME
Dept. Lab. Medicine and Pathology, SB-10, Univ. Washington Sch. Medicine, Seattle, WA, 98105
Hum Pathol; 12(9):771-772 1981

Attempt was made to explain the rapid development of malignant histiocytosis (MH) or histiocytic medullary reticulosis-like syndrome in the patients with acute lymphocytic leukemia and T cell lymphoma. The short interval between the start of therapy for leukemia and onset of the second disorder excluded the drug-induced etiology of histiocytosis. The chance coincidence of two diseases was also highly unlikely. Histologic and immunologic examination of the patients with MH accompanying acute leukemia showed an increasing number of histiocytes. The tumor cells had receptors for both unsensitized sheep RBC and IgG coated ox or sheep RBC indicating the lymphocyte subpopulation known as T gamma cells. (15 Refs)

## 8. RICHTER'S SYNDROME. EVIDENCE FOR THE CLONAL ORIGIN OF THE TWO PROLIFERATIONS.

Delsol G, Laurent G, Kuhlein E, Familiades J, Rigal F, Pris J
Laboratoire d'Anatomie Pathologique, C.H.U. Purpan, place du Dr. Baylac, 30159 Toulouse Cedex, France
Am J Clin Pathol; 76(3):308-315 1981

A case of Richter's syndrome was investigated by several technics: light and electron microscopy, surface markers, immunohistological studies and immunoelectron microscopy. On light microscopy lymph node proliferation was composed of large lymphoid cells, some exhibiting Reed-Sternberg like features. On electron microscopy many intermediary cells, from small lymphocytes to immunoblasts and plasma cells, were noted. The circulating small lymphocytes were characterized as B cells (SIg+; MRBC+). The lymph node cells shared the same SIg phenotype (IgMk) but the percentage of MRBC was slightly lower. Immunohistological studies showed that lymph node cells were stained exclusively by anti mu and anti kappa antisera. These results are indicative of the B clonal origin of the two cell proliferations. Immunoelectron microscopy showed three staining patterns: (1) cells presenting only surface staining, (2) cells with diffuse staining presumably related to ribosomal fixation, (3) cells with endoplasmic reticulum staining. The significance of these three patterns is discussed with regard to B lymphocyte differentiation. (Author abstract) (23 Refs)

## 9. SPECIFICITY AND POLYMORPHISM OF DIAMINOPEPTIDASE IV IN NORMAL AND NEOPLASTIC TTHETA LYMPHOCYTES.

Feller AC, Parwaresch MR
Inst. Pathology, Univ. Kiel, Hospitalstrasse 42, D-2300 Kiel, W. Germany
J Cancer Res Clin Oncol; 101(1):59-63 1981

A direct fluorometric assay showed the presence of diaminopeptidase IV (DAO IV) in two T-cell subsets from normal lymphocytes: the Tu fraction that binds IgM-Fc and the Tgamma fraction that binds IgG-Fc. Granulocytes, monocytes, and B lymphocytes were negative for the enzyme. In lymp hocytic leukemias, DAP IV activity was demonstrated in 10/17 T-cell acute lymphoblastic leukemias and 4/6 T-cell chronic lymphocytic leukemias. However, the activity was found only in the Tu subset. Thin-layer isoelectric focusing revealed identical DAP IV isoenzyme bands in normal peripheral blood T

lymphocytes as compared with that of acute and chronic T-cell leukemias. The enzyme activity was equally distributed among the isoenzyme loci. (23 Refs)

### 10. NUCLEOSIDE PHOSPHORYLASE ACTIVITY IN NORMAL AND LEUKEMIC CELLS.

Ben-Bassat I, Brok-Simoni F, Holtzman F, Ramot B
Inst. Hematology, Chaim Sheba Medical Center, Tel-Hashomer, Israel
Med Pediatr Oncol; 9(4):387-391 1981

Nucleoside phosphorylase (NP) activity was assayed in normal peripheral blood lymphocytes, mature and immature thymocytes fractionated by peanut agglutinability, CLL lymphocytes, and ALL lymphoblasts to determine applicability as an enzymatic cell marker. Circulating lymphocytes had the highest activity, immature thymocytes the lowest, and mature thymocytes were intermediate in NP level. This suggests an increase in NP activity with T-cell maturation. CLL lymphocytes showed very low activity, confirming previous reports. However, the NP activity of the lymphoblasts of 40 patients with B, T, and non-B, non-T ALL was similar to that of normal peripheral blood lymphocytes and could not be used to discriminate between these subgroups of ALL. (Author abstract) (24 Refs)

### 11. IMBALANCE OF T-CELL SUBPOPULATIONS DOES NOT RESULT IN DEFECTIVE HELPER FUNCTION IN CHRONIC LYMPHOCYTIC LEUKEMIA.

Inoshita T, Whiteside TL
(c/o Whiteside) Dept. Pathology, Univ. Pittsburgh, Sch. Medicine, 406 Scaife Hall, Pittsburgh, PA, 15261
Cancer; 48(8):1754-1760 1981

The T-lymphocyte subpopulations identified by the Fc receptors for IgG (TG cells) and IgM (TM cells) in 12 patients with B-cell chronic lymphocytic leukemia (CLL) were quantitated and studied for functional capabilities in an in vitro assay. The TG cells in patients were elevated in relation to age- and sex-matched normal controls (p less than 0.05) resulting in an altered TM/TG ratio of 1.8 +-0.76 in CLL versus 5.9 +-3.7 in controls (mean +- SD, p less than 0.001). Despite this altered TM/TG ratio, the functional capability of the CLL T cells to regulate the terminal differentiation of B cells was found to be normal as reflected by the mean helper-suppressor score of 0.77 +-0.13 (+- SEM) obtained for both patients and controls. This unimpaired capacity of the T cells from CLL patients to help normal B cells mature into Ig-secreting cells indicated that hypogammaglobulinemia and monoclonal serum Ig in these patients may be a result of either an intrinsic defect in the B lymphocytes or their replacement by a neoplastic clone rather than a defect in the immunoregulatory T cells. (Author abstract) (39 Refs)

### 12. THE STUDY OF THE BONE MARROW T-LYMPHOCYTES SUBSETS IN THE MULTIPLE MYELOMA PATIENTS.

Rizzo M, Meli C, Bonnano M, Maccarrone S, Guglielmo P
Cattedra di Ematologia, Universita di Catania, Catania, Italy
Boll Soc Ital Biol Sper; 57(6):678-684 1981

The purpose of this study was to find out, if the presence of the myelomatous B-monoclonal component could be associated to the changes in the T-dependent lymphocyte compartment. The 10 multiple myeloma (MM) patients (50-75 yr old) were compared with 12 normal controls. The total E-rosette forming T-cells (ERFC) were in the normal range (9.2 av MM, 10.3 av controls), except for one case with reduced value. Using West method quantitative distribution of the two main T-lymphocyte subsets was accomplished. High-affinity ERFC were reduced (2.13 av MM, 9.00 av controls) and low-affinity ERFC were increased (7.10 av MM, 3.00 av controls). Surface and intracytoplasmic immunoglobulins determination showed an inverse relationship between the B-monoclonal malignant component and low-affinity ERFC in all the patients. The predominance of the low-affinity T-subsets could play a role in the regulation of the myelomatous B-monoclonal component growth rate. (22 Refs) (In ITA)

## DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS

### 13. EXPRESSION OF 2 IMMUNOGLOBULIN ISOTYPES, IGM AND IGA, WITH IDENTICAL IDIOTYPE IN THE B CELL LYMPHOMA I.29.

Sitia R, Rubartelli A, Hammerling U
Dept. Immunology, Univ. Genoa, Viale Benedetto XV, 10, 16132 Genoa, Italy
J Immunol; 127(4):1388-1394 1981

The I.29 tumor originated in I strain mice as a B cell lymphoma. In its ascitic form, the cells express Ia and Lyb antigens and carry the Fc receptor. The tumor cells synthesize two Ig, IgM and IgA, which have lambda-chains and heavy chain idiotypic determinants in common. Double labeling of viable cells in immunofluorescence demonstrates that a majority of cells have only IgM (mu+), a proportion has only IgA (alpha+), and a small population (usually less than 5%) expressed both Ig isotypes (mu+ alpha+). Although the relative proportions of mu+, alpha+, and mu+ alpha+ cells fluctuate quite markedly in the serial passages of the tumor, the three different subpopulations are consistently observed. The proportion of cells binding fluorescein-labeled anti-mu and rhodamine-labeled anti-alpha simultaneously in the cytoplasm is slightly higher (less than 10%). The appearance of cytoplasmic staining as brightly fluoresceinating granules suggests sequestration of Ig, possibly into vesicles. In vitro culture of I.29 cells rapidly leads to preferential expression of IgA only. This conversion from IgM- to IgA-producing cells was also observed when cultures were initiated with highly purified IgM+IgA- I.29 cells, suggesting differentiation rather than selective growth as the cause of the change. Cloning of I.29 cells by the limiting dilution technique yielded only cell lines of IgM-IgA+ phenotype. Implantation of one such cell line in nude mice produced a tumor that retained this phenotype in successive passages. (Author abstract) (57 Refs)

### 14. DISTRIBUTION OF IGG AND IGM RECEPTORS ON HUMAN PERIPHERAL NATURAL KILLER CELLS MEASURED ON THE LEVEL OF SINGLE EFFECTOR CELL.

Jondal M, Merrill JE
Dept. Tumor Biology, Karolinska Institutet, S-104 01 Stockholm, Sweden
Eur J Immunol; 11(7):531-535 1981

Using an agarose single-cell cytotoxicity assay simultaneously with the antibody-coated ox RBC assay for detecting Fc receptor (FcR)-positive cells, the number of natural killer (NK) cells in fresh human peripheral blood which bear FcR for IgG or IgM have been determined. Of the target binding cells

(TBC) which form conjugates with NK-sensitive target cell lines Molt 4, 1301 and Hd-Mar, 55% had FcR for IgG and 24% had FcR for IgM. In the active NK cell population, which amounts to about 6% in nylon wool column-passed peripheral lymphocytes, cells with FcR for IgG account for 60% and cells with FcR for IgM for 17% of the total killing. Even though there is an increase in the number of FcR-IgM-positive cells from fresh peripheral blood after overnight incubation at 37 C, no increase was found in FcR-IgM-positive NK cells. The reasons why FcR for IgM have not been described earlier on human NK cells are discussed, as well as the functional implications of these and their probable expression on other types of cytotoxic effector cells. (Author abstract) (32 Refs)

## 15. INFLUENCE OF IGG AND IGM RECEPTOR TRIGGERING ON HUMAN NATURAL KILLER CELL CYTOTOXICITY MEASURED ON THE LEVEL OF THE SINGLE EFFECTOR CELL.

**Merrill JE, Ullberg M, Jondal M**
**Dept. Tumor Biology, Karolinska Institutet, S-104 01 Stockholm, Sweden**
**Eur J Immunol; 11(7):536-541 1981**

By using an agarose single cell cytotoxicity assay, in combination with rosetting with IgG- or IgM-coated ox RBC for detection of Fc receptors for IgG (FcgammaR) or IgM (FcmuR), it was found that 60% of natural killer (NK) cells are FcgammaR+ and 17% FcmuR+. This system was further used to investigate the consequence of FcuR and FcgammaR triggering on NK killing as measured on the single effector cell level. It was found that stimulation of the FcgammaR, but not the FcmuR, resulted in substantial NK inhibition. In order for NK cells to be inhibited by IgG-coated ox RBC, they must first be exposed to the IgG-containing complex prior to conjugation with the target. While exposure of the FcgammaR to immune complexes can block up to 57% of NK activity, the particulate immune complexes do not interfere with binding of effector cells to targets. Modulation of FcgammaR by capping at 37 C does not interfere with the NK inhibition for up to 3 hr, though after 20 hr, when FcgammaR+ cells are almost completely modulated, NK activity has fully returned. Although to a lesser extent, the soluble immune complex human transferrin-anti-transferrin also reduces NK cell activity when activating effector cell FcgammaR prior to target cell binding. Also, pretreatment of target cells with high concentrations of specific antibody toward membrane antigens can block NK activity while not inhibiting target cell binding as evidenced by anti-IgM IgG binding to Daudi cells. The regulatory influence of the FcgammaR on the NK system is discussed in terms of other functions associated with this receptor and in terms of its possible biological significance. (Author abstract) (25 Refs)

## 16. COMPLEMENT RECEPTORS ON LYMPHOCYTES.

**Dierich MP**
**Hygiene-Institut der Univsersitat, Obere Zahlbacher Strasse 67, D-6500 Mainz, W. Germany**
**J Cancer Res Clin Oncol; 101(1):65-67 1981**

Complement (C)-coated sheep RBC (EA) were used to specify the C receptor activity of lymphocytes. RBC carrying C3b, C3bi, or C3d were used to specify the complement receptor activity of lymphocytes. Peripheral blood WBC interacted with all three cell types: EAC1-3b, 15% rosettes, EAC1-3bi, 18% rosettes, and EAC1-3d, 12% rosettes. After the elimination of monocytes and most T cells, peripheral blood WBC formed rosettes with 45%, 55% and 50%, respectively. Among Burkitt lymphoma-derived cell lines, Raji cells formed rosettes with 25%, 90% and 90%, respectively. Cells from the Daudi line did not interact with EAC1, but they reacted with C3bi-(70%) and C3d-(90%) cells. Human RBC reacted only with C3b-coated cells, whereas human monocytes and granulocytes were positive for both C3b- and C3bi- cells. The role of factor H (beta 1H) in the binding of C3bi is discussed. (10 Refs)

## 17. IMMUNOHISTOLOGICAL DEMONSTRATION AND PHYSIOCHEMICAL CHARACTERIZATION OF C3 RECEPTORS OF NORMAL AND NEOPLASTIC LYMPHOID CELLS.

**Gerdes J, Stein H**
**Inst. Pathology, Univ. Kiel, Hospitalstrasse 42, D-2300 Kiel, W. Germany**
**J Cancer Res Clin Oncol; 101(1):69-74 1981**

Complement 3 (C3) receptor-positive cells on frozen sections of human tonsil tissue and lymph node tissue from patients with malignant lymphoma were demonstrated by the immunoperoxidase staining of the sections with an anti-C3 receptor serum (AC3RS). In the tonsil tissue, the immunostaining was confined to germinal center cells, follicular mantle cells, and a few interfollicular cells. AC3RS stained the neoplastic follicles in a centroblastic-centrocytic lymphoma and the nonneoplastic follicles in a T-zone lymphoma; the neoplastic T cells in this lymphoma did not react with the antiserum. Two sets of experiments were performed to clarify discrepancies in the results of mol wt analyses of C3 receptors. When tonsillar lymphocyte membrane fractions were solubilized and then radioiodinated, two components with mol wt of 38,000 and 18,000 were precipitated with AC3RS. When whole cells were tritiated and then solubilized, only one component with a mol wt of 200,000 was precipitated with the antiserum. These results suggested that the discrepancies were due to the different methods of lysate preparation or labeling. (10 Refs)

## 18. E-ROSETTE FORMATION IN B-CELL LYMPHATIC LEUKEMIAS INDUCED BY BINDING ACTIVITY OF MONOCLONAL SURFACE IMMUNOGLOBULINS TO SHEEP RED BLOOD CELLS.

**Mitrou PS, Bergmann L, Holloway K, Zerth G**
**Dept. Internal Medicine, Div. Hematology/Oncology, Johann Wolfgang Goethe Univ., Frankfurt, W. Germany**
**Clin Immunol Immunopathol; 20(3):346-353 1981**

The cells of a chronic lymphocytic leukemia (CLL) and a prolymphocytic leukemia (PLL) formed rosettes with sheep RBC (SRBC) and expressed characteristic surface markers of B cells, ie, monoclonal surface IgM, Ia-like antigen, and receptors for aggregated IgG. Rosette formation was demonstrated to be the result of binding activity of surface Ig to SRBC. Pretreatment of the leukemic cells with Pronase, or antibodies to mu, lambda, or kappa, chains, respectively, completely inhibited rosette formation with SRBC. Preincubation of SRBC with serum of IgM fraction of the patient with PLL decreased rosette formation demonstrating circulating antibodies to antigen(s) on SRBC. The serum and IgM fraction of the patient with CLL agglutinated and lysed SRBC. The antigen(s) on SRBC involved in rosette formation were not related to Forssman or Paul Bunnel antigen. (Author abstract) (20 Refs)

### 19. MODIFIED E ROSETTE TEST IN WOMEN WITH MALIGNANT OVARIAN NEOPLASMS.

Simm S, Tomaszkiewicz T, Markowska J, Kominek P
Klinika Onkologii, Akademia Medyczna, ul. Lakowa 1/2, 61-878 Poznan, Poland
Ginekol Pol; 52(3):225-230 1981

Routine and modified E rosette tests were performed in 26 women with malignant ovarian tumors. Sixteen patients were in Stages I-III (Group 1), and 10 in Stage IV (Group 2). In the modified tests the rosette formation was determined in the presence of tumor-specific antigen (test A) or of the patient's blood serum (test B). The percentage E rosettes, determined by the routine test, was 502% (44.9% in Group 1 and 58.6% in Group 2) vs 56.5% in 22 controls. Test A showed 34% E rosettes in the patients (26.9% in Group 1 and 45.4% in Group 2), while test B revealed 52.1% E rosettes in the patients (48.1% in Group 1 and 57.4% in Group 2). The modified test methods permitted to discern a subpopulation of T lymphocytes, sensitized to tumor antigen, and to calculate the percentage of rosettes responsible for the general immunity. (18 Refs) (In POL)

### 20. BIOCHEMICAL CHARACTERIZATION OF SYRIAN HAMSTER CELL SURFACE ALLOANTIGENS. III. H AMSTER ALLOANTISERA IMMUNOPRECIPITATE CLASS II-LIKE, BUT NOT CLASS I-LIKE, MOLECULES.

Streilein JW, Phillips JT, Stein-Streilein J, Proia DA, Duncan WR
Dept. Cell Biology, Univ. Texas Health Science Center at Dallas, Dallas, TX, 75235
Transplantation; 32(2):106-110 1981

Indirect immunoprecipitation of 12 hamster alloantisera, recently produced by mutual immunizations of domestic inbred strains and recently wild, partially inbred lines, demonstrated that all immunoprecipitates comprise only two species of molecules: one of approx mol wt of 29,000 and the other 39,000 daltons. Surface alloantigens were immunoprecipitated from lymphocyte glycoprotein fractions obtained from every hamster strain tested: MHA, UT1, UT2, MIT, and TX/. In no instance was either component detected alone and no other molecules of different mol wt were found. The expression of these cell surface molecules only on spleen and lymph node cells suggests that hamster T cells display cell surface class II homologues. Putative hamster homologues of class I MHC molecules were not identified by any of the antisera. The hypothesis that hamsters possess a chromosomal region, tentatively designated Hm-1, that comprises genetic loci encoding alloantigens detectable by mixed lymphocyte reactivity and by serology, a region that resemble the I region of murine H-2, is proposed. (27 Refs)

### 21. ROLE OF T-CELLS IN THE MECHANISM OF REACTIVITY OF THE MICROPLATE LEUKOCYTE ADHERENCE INHIBITION ASSAY.

Raina S, Russo AJ, Jenkins D, Goldrosen MH
(c/o Goldrosen) Dept. Surgical Oncology, Tumor Immunology Lab., Roswell Park Memorial Inst., Buffalo, NY, 14263
Cancer Res; 41(10):3950-3955 1981

To characterize the role of mononuclear cells in the microplate leukocyte adherence inhibition assay, enriched populations of T-cells, B-cells, macrophages, and a nylon wool-adherent fraction consisting of B-cells and macrophages were prepared by a two-stage adherence procedure from spleen cells of normal C57BL/6J mice and mice bearing progressively growing murine colon adenocarcinoma 38 (MCA-38) tumors. These studies indicate that the reactive cell undergoing specific antigen-induced adherence inhibition was present in the macrophage fraction. This cell was programmed to undergo specific antigen-induced adherence inhibition by an MCA-38-sensitized B-cell. An enriched population of MCA-38 reactive cells. Pretreatment of the MCA-38-sensitized T-cell fraction with anti-Thy 1:2 serum and complement but not anti-Ig and complement or carbonyl iron to selectively deplete macrophages abolished the regulatory effect of the MCA-38-sensitized T-cell fraction. MCA-38-sensitized T-cells could prevent MCA-38-sensitized B-cells from programming normal macrophages in vitro but could not abolish the leukocyte adherence inhibition response of presensitized macrophages. Temporal studies of suppressor T-cell activity were performed throughout different phases of progressive tumor growth. Suppressor T-cells could be detected as early as 4 days post-MCA-38 tumor cell inoculation and persisted throughout MCA-38 progressive tumor growth. Titration studies of suppressor T-cells revealed the need for 4x the number of MCA-38-sensitized T-cells from small tumor bearers (day 4) in comparison to large tumor bearers (day 20) to achieve the same degree of suppression. Thus, in the MCA-38 system, sensitized T-cells exert a negative regulatory influence by preventing B-cell programming of normal macrophages. This negative regulatory influence increased in magnitude with the progressive growth of the MCA-38 tumor. (Author abstract) (25 Refs)

## LYMPHOCYTE AND DIFFERENTIATION ANTIGENS

### 22. QUANTITATIVE IMMUNOFLUORESCENT ANALYSIS OF SURFACE PHENOTYPES OF MURINE B CELL LYMPHOMAS AND PLASMACYTOMAS WITH MONOCLONAL ANTIBODIES.

Lanier LL, Warner NL, Ledbetter JA, Herzenberg LA
Immunology Lab., Dept. Pathology and Medicine, Univ. New Mexico Sch. Medicine, Albuquerque, NM, 87131
J Immunol; 127(4):1691-1697 1981

In this study, a large series of murine B lymphomas and plasmacytomas were examined by quantitative flow cytometry analysis using a panel of monoclonal antibodies against murine differentiation antigens. These cell lines appear to represent subpopulations of lymphoid cells arrested at distinct stages of differentiation. In general, the pattern of reactions of these monoclonal antibodies with the B cell neoplasms was comparable to the reactions seen with normal cells in the same lineage. The Thy-1.2, Lyt-2, and T-30 differentiation antigens were not detected on any B lymphoma or plasmacytoma. However, certain surface Ig-positive B lymphomas do express the Lyt-1 antigen. With respect to other differentiation markers examined, including E2, F1, ThB, Lgp-100 (Ly 9.1), G2, and T-200 (Ly 5), the reaction of the B cell tumors reflected the expression of these markers on comparable normal cells. This investigation also emphasized the marked intratumor and intertumor heterogeneity that is observed when cloned cell lines are analyzed quantitatively for a large number of surface markers. Thus, this approach may be particularly useful in defining heterogeneity in maturation states within cloned tumor cell lines. (Author abstract) (33 Refs)

## 23. CHARACTERIZATION, BY IMMUNOPRECIPITATION, OF MYELOID- AND MONOCYTE-SPECIFIC ANTIGENS PRESENT ON THE HUMAN PROMYELOCYTIC CELL LINE (HL-60) IN THREE STAGES OF DIFFERENTIATION.

Mulder A, Alexander S, Engelfriet CP, Von dem Borne AE, Strominger JL
Dept. Immunohaematology, Central Lab. Netherlands Red Cross Blood Transfusion Service, Univ. Amsterdam, Amsterdam, The Netherlands
Proc Natl Acad Sci USA; 78(8):5091-5095 1981

The human promyelocytic leukemia cell line HL-60 is reactive with an antiserum raised against normal human granulocytes (AGS). Immunoprecipitation with AGS on [35S]methionine-labeled HL-60 cell lysates with subsequent analysis by NaDodSO4/polyacrylamide slab gel electrophoresis shows a major antigenic doublet with mol wt of 88,000 and 86,000, together with some minor antigens of lower mol wt. Upon stimulation with dimethyl sulfoxide or 12-O-tetradecanoylphorbol 13-acetate, which induces HL-60 to differentiate to mature granulocytes or monocytes/macrophages, respectively, this antigenic doublet disappears. 12-O-Tetradecanoylphorbol 13-acetate induces the synthesis of an antigen, mol wt 83,000, reactive with an antimonocyte serum. Neutrophil-specific alloantigens were not detected on HL-60 or its differentiated derivatives. (Author abstract) (29 Refs)

## 24. SURFACE MEMBRANE ANTIGENS OF HEMOPOIETIC TUMOR CELL LINES AND NORMAL MARROW PROGENITOR CELLS.

Hasthorpe S, Rogerson J, McKenzie IF
Cancer Inst., 481 Little Lonsdale St., Melbourne, 3000, Australia
Cancer Res; 41(10):3985-3991 1981

A xenoantiserum raised against a mast cell tumor line (FMP1.1) was found to have cross-reactivity with surface antigens on primitive hemopoietic precursor cells in normal mouse bone marrow: erythroid burst-forming units; granulocyte-macrophage colony-forming cells; and high-proliferative-potential granulocyte-macrophage colony-forming cells. In the presence of anti-FMP1.1 serum and complement, only 15 +-2% (S.E.) (n = 5) of normal nucleated marrow cells were lysed, demonstrating that the majority of mature hemopoietic cells did not express the antigens detected on their primitive counterparts. A variety of hemopoietic and other tumor cell lines were examined with anti-FMP1.1 serum, and all B- and pre-B-lymphomas, one plasmacytoma, one mastocytoma, and a monocyte-macrophage line exhibited significant lysis. Direct typing of the FMP1.1 tumor demonstrated that it did not express the B-cell surface antigens such as Ia, surface Ig, Fc, and complement (C3) receptors. Although the Ly.6 alloantigen was present on FMP1.1 cells, this antigen was not found on marrow erythroid burst-forming units and granulocyte-macrophage colony-forming units. Absorption of anti-FMP1.1 serum with cross-reacting (WEHI-3 and W-279.1) and a nonreacting (P-815) cell line confirmed the specificity of the antiserum reaction with these cells and marrow progenitors. These experiments indicated that more than one antibody is contained in anti-FMP1.1 serum. Thus, the mast cell tumor (FMP1.1) carries an unusual array of antigens, which are found on bone marrow progenitors and are not expressed on the majority of differentiated cells. It has been demonstrated that tumor cell lines provide an important basis for the analysis of surface membrane antigens expressed on normal hemopoietic progenitors. (Author abstract) (29 Refs)

## 25. CELL HYBRIDIZATION: A MONOCLONAL MARKER AS A DIAGNOSTIC AID IN HEMATOLOGY AND ONCOLOGY.

Tilz GP, Beverley P, Becker H, Lanzer G, Sedlmayr P
Medizinische Universitatsklinik, Auenbruggerplatz 15, A-8036 Gratz, Austria
Acta Med Austriaca; 8(3):85-87 1981

A monoclonal marker for hematologic and oncologic purposes was developed. Male BALB/c mice were immunized sc with 4.5 x 10(6) human lymphocytes and boosted ip at monthly intervals with 2-5 x 10(6) of the same type cells. Four days after the last booster dose, spleen cells were obtained from the mice and fused with NS-1 plasmacytoma cells. Polyethylene glycol (40% soln) was used as a fusing agent. Cells were grown on selective heterophilic antibody titer medium. Cells were selected and cloned on the basis of antibody production. Clones were tested for antibody activity against infantile thymus, lymph node, tonsil, bone marrow, and various solid tumor tissues, as well as leukemic and erythroleukemic cells. One IgG 1-producing clone was identified that reacted with lymphoid cells, band cells, polymorphs, eosinophils, and macrophages. The clone did not react with erythropoietic cells or with undifferentiated carcinoma cells. It was designated H Le D 1. Use of this clone allows differential diagnosis of undifferentiated carcinomas and lymphoid malignancies. (10 Refs) (In GER)

## 26. DEMONSTRATION OF A CORRELATION BETWEEN TUMOR CELL H-2 ANTIGEN CONTENT, IMMUNOGENICITY, AND TUMORIGENICITY USING LECTIN-RESISTANT TUMOR VARIANTS.

Dennis JW, Donaghue TP, Carlow DA, Kerbel RS
(c/o Kerbel) Cancer Res. Div., Dept. Pathology, Queen's Univ., Kingston, Ontario K7L 3N6, Canada
Cancer Res; 41(10):4010-4019 1981

Four wheat germ agglutinin-resistant (WGAR) variants of the highly malignant murine tumor MDAY-D2 were examined for membrane alterations which might correlate with their decrease in tumorigenicity described previously. Injection sc of as many as 5 x 10(6) cells of the WGAR variants MDW1 or MDW3 was rejected by the normal syngeneic DBA/2 host, but they grew rapidly and progressively in athymic nude mice, suggesting that a vigorous T-cell-mediated immune response was responsible for rejection of the variants in the immunocompetent host. In contrast, an inoculum of as few as 10(2) MDW4, MDW5, or MDAY-D2 cells gave rise to progressively growing metastatic tumors in normal DBA/2 mice. Hence, the MDW1 and MDW3 variants appeared more immunogenic than did the MDW4, MDW5, or MDAY-D2 parent tumor. Two lines of evidence suggested that all of the WGAR variants and parental tumors shared a common tumor-associated antigen; (a) rejection of MDW1 tumor cells by DBA/2 mice immunized them against a subsequent challenge of either MDAY-D2 or MDW4 cells; (b) antitumor cytotoxic T-lymphocyte (CTL) activity was detected in a 4-hr 51Cr release assay in spleens taken from tumor-bearing mice and restimulated in vitro with mitomycin C-treated tumor cells. MDAY-D2 and WGAR variants were cross-reactive, both as immunogens at the restimulation stage and as CTL targets. Compared to the tumorigenic lines, MDW1 and MDW3 were more effective stimulators of tumor-specific CTL and were superior targets in the CTL assay. Similarly, stimulation of syngeneic DBA/2 spleen cells with trinitrophenol-modified tumor cells showed MDW1 and MDW3 were more effective stimulators of the trinitrophenyl-specific response and were more readily lysed

by trinitrophenyl-directed CTL than were the other WGAR variants or MDAY-D2. Separation of microsomal membrane proteins on sodium dodecyl sulfate:polyacrylamide gel electrophoresis revealed an elevated level of two glycoproteins with apparent mol wt of 43,000 and 47,000, present in the microsomes of MDW1 and MDW3. The glycoproteins were identified as H-2D and H-2K, respectively. Absorption of alloantiserum by whole tumor cells indicated that the WGAR variants and MDAY-D2 had similar amounts of H-2 on their cell surface. In contrast, absorption tests, using tumor cell endoplasmic reticulum and plasma membrane fractions, as well as analysis of the membrane fractions by sodium dodecyl sulfate:polyacrylamide gel electrophoresis, showed an increased level of H-2 in the endoplasmic reticulum of the MDW1 and MDW3 variants. The results demonstrate an inverse correlation between the tumorigenicity and both the immunogenicity and cellular H-2 levels of the variant tumor cell lines. (Author abstract) (37 Refs)

### 27. CELL-SPECIFIC CYTOTOXICITY EXPRESSED BY A CONJUGATE OF RICIN AND MURINE MONOCLONAL ANTIBODY DIRECTED AGAINST THY 1.1 ANTIGEN.

**Houston LL, Nowinski RC**
**Dept. Biochemistry, Univ. Kansas, Lawrence, KS, 66045**
**Cancer Res; 41(10):3913-3917 1981**

The isolation and characterization are described of a conjugate between ricin and a Thy 1.1-specific monoclonal IgG2a murine antibody synthesized using N-succinimidyl-3-(2-pyridyldithio)propionate. The conjugate selectively inhibited protein synthesis in Thy 1.1-positive (AKR SL3) mouse leukemia cells compared to Thy 1.2-positive (AKR/Cu SL1) cells. (Author abstract) (17 Refs)

## CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION

### 28. T CELLS WITH FC RECEPTORS FOR IGA: INDUCTION OF TALPHA CELLS IN VIVO AND IN VITRO BY PURIFIED IGA.

**Hoover RG, Dieckgraefe BK, Lynch RG**
**(c/o Lynch) Dept. Pathology (ML-144), Univ. Iowa Hosp., Iowa City, IA, 52242**
**J Immunol; 127(4):1560-1563 1981**

Previous studies demonstrated that BALB/c mice with the IgA-secreting plasmacytomas MOPC-315 (alphalambda2), MOPC-167 (alphakappa), McPC-603 (alphakappa) and TEPC-15 (alphakappa) developed large numbers of T cells with surface membrane receptors for IgA (Talpha cells). The lack of Talpha cell expan sion in mice with variant plasmacytomas that were nonsecretors or low secretors of IgA implied that elevated serum IgA contributed to the increase in Talpha cells. The present studies showed that normal BALB/c mice that were given daily injections of 30 mg of IgA (M315 protein) develop a marked increase in the number of Talpha cells. These studies also show that the Talpha cells induced by injection of IgA are Lyt1-2+ T cells. In addition, the data presented demonstrate that nylon wool nonadherent T cells, treated with purified polymeric IgA (M315 protein) in vitro, develop a marked increase in the number of Talpha cells. The in vitro induction of Talpha cells by IgA requires DNA and protein synthesis. These findings indicate that Talpha cell expansion observed in mice with IgA myeloma is related to the high serum level of IgA and not to the myeloma tumor per se. In addition, these observations have a more general relevance to the issue of B cell regulation because they demonstrate that secreted Ig can directly induce expansion of immunoregulatory T cells. (Author abstract) (17 Refs)

### 29. RECOGNITION OF MOPC-460 VARIABLE REGION DETERMINANTS BY POLYCLONALLY DISTRIBUTED TRIGGERING RECEPTORS ON B LYMPHOCYTES.

**Primi D, Juy D, Le Guern C, Sanchez P, Cazenave PA**
**Unite d'Immunochimie Analytique, Institut Pasteur, 28 rue du Dr. Roux, 75724 Paris Cedex 15, France**
**J Immunol; 127(4):1714-1718 1981**

Purified M460 protein-induced untreated and anti-Thy 1.2 and complement-treated murine spleen cells to proliferate and differentiate in vitro. Fc receptor complexing was not responsible for the phenomenon, since M460 Fab fragments retained the B cell triggering activity. Activation was inhibitable by the addition of DNP-glycine to cultures and could also be detected by using spleen cells from various strains of mice, including the C3H/HeJ, which is genetically nonresponding to LPS. Hybrid molecules were constructed between the M460 proteins and the products of two myelomas that do not activate B cells, namely, X25 and X24. The only hybrid molecules that retained triggering activity were (L460-HX25)2. Interestingly, the same molecule was also the only one recognized by an anti-M460 monoclonal antibody (F6(51)) that has been previously shown to induce B cells to proliferate and differentiate. The data suggest the existence on B lymphocytes of a network of polyclonally distributed mitogen receptors that share determinants cross-reacting with Ig idiotypes. (Author abstract) (21 Refs)

### 30. DEMONSTRATION WITH MONOCLONAL ANTIBODIES OF AN UNUSUAL MONONUCLEAR CELL INFILTRATE AND LOSS OF NORMAL EPITHELIAL MEMBRANE ANTIGENS IN HUMAN BREAST CARCINOMAS.

**Daar AS, Fabre JW**
**Nuffield Dept. Surgery, Univ. Oxford, John Radcliffe Hosp., Oxford OX3 9DU, England**
**Lancet; 2(8244):434-438 1981**

Monoclonal antibodies to two differentiation antigens normally expressed on the membranes of breast epithelial cells were used in immunofluorescence studies on frozen sections of malignant breast tumors. It was demonstrated that most tumors did not express these antigens on their cell membranes, and it was possible to classify histologically indistinguishable tumors according to whether they expressed the antigens. The absence of these membrane antigens is likely to be a subtle indicator of cellular differentiation and to have metabolic and other functional implications for the tumor. The demonstration that otherwise indistinguishable tumors can be classified in this way therefore has obvious potential for clinical exploitation. In addition, it was demonstrated that the majority of the mononuclear cells in those tumors with intense mononuclear cell infiltrates expressed an antigen not normally found on mature lymphocytes and macrophages. (Author abstract) (11 Refs)

## EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS

### 31. FORMATION OF IGE-BINDING FACTORS BY RAT T LYMPHOCYTES. I. INDUCTION OF IGE-BINDING FACTORS BY POLY I:C AND INTERFERON.

**Yodoi J, Hirashima M, Bloom BR, Ishizaka K**
**Dept. Medicine, Johns Hopkins Univ. Sch. Medicine, Good Samaritan Hosp., Baltimore, MD, 21239**
**J Immunol; 127(4):1579-1585 1981**

Rat serum obtained 8 to 18 hr after an ip injection of poly I:C contained IgE-binding factors, which can be detected by the inhibition of rosette formation of FcepsilonR(+) cells with IgE-coated RBC. Incubation of normal rat spleen cells with 1 ug/ml poly I:C resulted in the formation of IgE-binding factors. Approx one-half of the IgE-binding factors in the culture supernatant were IgE-potentiating factors, which have affinity for concanavalin A (Con A), whereas the remaining half of the factors were IgE-suppressive factors with no affinity for the lectin. Culture supernatants of poly I:C-stimulated spleen cells as well as the serum of poly I:C treated rats contained not only IgE-binding factors but also soluble factors that induce normal lymphocytes to form IgE-binding factors. It was found that poly I:C-stimulated splenic adherent cells and peritoneal macrophages formed soluble factors, which in turn induced T lymphocytes to express FcepsilonR and to form IgE-binding factors. The inducers derived from poly I:C-stimulated cells failed to augment the expression of FcepsilonR on B cells. The soluble factors could induce the formation of both IgE-potentiating factors and IgE-suppressive factors. Upon incubation with the inducers, 10 ug/ml Con A-activated cells formed IgE-potentiating factors; 1 ug/ml Con A-activated cells formed IgE-suppressive factors. The inducers had affinity for polyuridylic acid and blue dextran Sepharose, and could be recovered from the beads by elution with 1 M NaCl. It was also found that supernatant of mouse spleen cells co-cultured with virus-infected HeLa cells induced normal rat lymphocytes to form IgE-binding factors. The inducers in the culture supernatants were neutralized by a minute dose of antibodies specific for mouse Type I interferon, indicating that mouse interferon can induce the formation of IgE-binding factors. (Author abstract) (40 Refs)

### 32. IN VIVO AUGMENTATION OF NATURAL KILLER (NK) ACTIVITY BY A STREPTOCOCCAL PREPARATION, OK-432: CHARACTERIZATION OF EFFECTOR CELLS AND INDUCTION OF INTERFERON IN SERA.

**Wakasugi H, Miyata M, Morioka Y, Oshimi K, Kasahara T, Takahashi K, Saito M, Ebina T**
**Dept. Surgery, Jichi Medical Sch., Japan**
**Nippon Gan Chiryo Gakkai Shi; 16(3):433-446 1981**

The effects of pre- and/or postoperative treatment with streptococcal preparation OK-432 on natural killer (NK) cell activity and interferon titers were studied in 40 patients with stomach, breast, pancreas, or colon cancer. The patients received a first OK-432 course beginning on postoperative days 7-35 (Group I) or a second course beginning on postoperative days 8-52 (Group II), 6-20 (Group III), or 5-43 (Group IV). Patients in Groups I, II, and III showed significantly augmented killer cell activity within 3 days of initial OK-432 inoculation. Characterization of effector cells from Group IV patients showed that they were NK cells (T and non-T cells and IgG-Fc receptor-positive cells). Induced IF titers studied in Groups I, II, and III did not correlate with levels of augmented NK activity. Four Group III subgroups were distinguished according to degree of NK activity and IF titers: patients with low IF titers that declined with augmented NK activity, patients with low titers that increased with augmented NK activity, patients in whom IF was detected continuously without NK augmentation, and patients with augmented NK activity but no significant IF induction. (40 Refs) (In JPN)

### 33. IMMUNOLOGICAL FACTORS CORRELATED IN RADIATION EFFECT IN CANCER PATIENTS TREATED BY RADIOTHERAPY ALONE OR RADIOTHERAPY WITH COMBINED CHEMOTHERAPY.

**Kimura S**
**Dept. Radiology, Kobe Univ. Sch. Medicine, Kobe, Japan**
**Nippon Iguku Hoshasen Gakkai Zasshi; 41(6):559-573 1981**

Clarifying the influence of irradiation on tumor-host relationship is important to improve the effect of radiotherapy in cancer patients. We have tried to search for the correlation between local as well as systemic immunological factors and radiation effect. Local immunological factors are thought to be parenchymal reaction of normal and tumor tissues. These were studied by morphological changes of angiographic findings and histological methods which included photomicroscopic, electron-microscopic and enzyme-histochemical studies. It was demonstrated that the effect of radiotherap y depended on not only local blood supply but also parenchymal reaction of the host. Especially, the parenchymal reaction at 2,000 or 3,000 rad irradiation was regarded as nonspecific tissue repair as well as immunological protective reactions brought about by enhancement of the tumor antigenicity. It was proved that the T-cell system played a main role in this parenchymal reaction. Changes of systemic immunological factors were studied in 17 laryngeal cancer and 80 lung cancer patients treated by radiotherapy alone or radiotherapy with combined chemotherapy. Due to the fact that damages of the host before treatment were not so serious and integral dose given to the patients was a little, in cases of laryngeal cancer immunological parameters such as absolute lymphocyte counts, PHA and PPD skin test activities, lymphocyte blastoid transformation with PHA, PWM and Con A, did not show significant change. However, as for lung cancer treated by large integral dose irradiation combined with chemotherapy, immunological parameters were depressed in inverse proportion to the dose of irradiation and chemotherapeutic agents. Moreover T-cell subsets (early E-rosette forming cells, IgG Fc-receptor positive cells), lymphocyte sub-populations, ADCC activity, serum immunoglobulins, and serum protein were also investigated in cases of lung cancer. We have evaluated the immunological parameters in relation to the therapeutic effect. As a result, it was suggested that several parameters should be needed to forecast the prognosis. The influence of immunopotentiator on immunological parameters and prognosis was investigated in lung cancer. The suppression of some immunological parameters was reduced in immunopotentiators administered group compared with non-administered group. Through no statistical significance was shown, some elongation of survival time was demonstrated in the immunopotentiator-administered group. As a result, immunopotentiators indicated the tendency to prevent immunocompetence of lymphocytes from suppression. Secondary immunodeficiency often occurs during radiotherapy with combined chemotherapy. It is valuable to examine some immunological parameters to avoid immunodeficiency during and after radiotherapy with combined chemotherapy. (Author abstract) (32 Refs) (In JPN)

### 34. LONG-TERM EFFECT OF POSTOPERATIVE IRRADIATION ON THE IMMUNE FUNCTIONS IN PATIENTS WITH MAMMARY CARCINOMA.

**Toivanen A, Nordman E**
**Dept. Medicine, Medical Microbiology and Radiation Therapy, Univ. Turku, SF-20520 Turku, Finland**
**Acta Radiol Oncol Radiat Phys Biol; 20(2):119-124 1981**

The effect of postoperative irradiation on the immune functions of 13 patients with breast carcinoma is reported, using as parameters the peripheral blood lymphocyte count, percentages of E and EAC rosette forming cells, and lymphocyte proliferative responses to PHA, Con A and PPD. After irradiation the number of peripheral blood lymphocytes was reduced during 8 mo. The percentages of E and EAC rosette forming cells were not altered during the observation time of 7 to 36 mo. In the proliferative responses of lymphocytes to PHA, Con A and PPD, the postoperative irradiation caused a decrease which, regarding PHA and Con A, lasted up to 8 mo and then recovered. The decrease in the proliferative responses to PPD was stronger and lasted during the whole observation time. In the mitogenic responses of patients with recurrent or disseminating disease no difference could be demonstrated as compared with the patients living recurrence-free. (Author abstract) (24 Refs)

### 35. CELL-MEDIATED IMMUNITY INDICES IN PATIENTS WITH RECTAL TUMORS AFTER SURGERY AND COMBINED THERAPY.

**Evsev'eva AI, Mosienko MD, Zybina MA, Umansky YuA**
**R. E. Kavetsky Inst. Oncology of Acad. Sciences of Ukrainian SSR., Kiev, USSR**
**Vopr Onkol; 27(6):40-44 1981**

The dynamics of cell-mediated immunity indices in 83 patients with rectal tumors who underwent surgery or received combined treatment (preoperative radiation and surgery) was followed. Cellular immunity was assessed on the basis of PHA-induced blastogenic reaction of lymphocytes (BRL) and spontaneous rosette-formation. In rectal tumor patients, particularly at Stage IV, the level of PHA-induced BRL and the total number of rosette-forming cells (RFC) were lower than in healthy donors. Surgery did not produce any significant changes in cell-mediated immunity parameters: level of PHA-induced BRL decreased by 16,7%, while total RFC number increased by 17.2% (mostly low-affinity forms). Preoperative radiation resulted in a significant decrease in lymphocyte ability to undergo PHA-induced blast-transformation (45%) and spontaneous rosette formation, high-affinity lymphocytes being most sensitive to ionizing radiation. Their fraction decreased by half. (Author abstract) (18 Refs) (In RUS)

### 36. CYTOCHEMICAL AND IMMUNOLOGICAL PROPERTIES OF CRYOPRESERVED BLAST CELLS.

**Delfini C, De Biagi M, Polchi P, Nesci S, Valentini M, Lucarelli G**
**Divisione di Ematologia, Ospedale Riuniti, Pesaro, Italy**
**Haematologica (Pavia); 66(2):151-159 1981**

The ability of frozen-thawed pathological cells to retain their cytochemical properties and the influence of cryogenic preservation on T and B cell surface markers and on the DNA synthesis of blast cells from acute (ALL) and chronic (CLL) leukemias were evaluated. Peripheral blood and bone marrow cells from 10 untreated patients with ALL and CLL were examined. Fetal calf serum appeared to be an important factor for cell protection during the freezing and thawing phases. A satisfactory percentage of cells (av 50%) was achieved using 10% fetal calf serum. The effect of the freezing-thawing procedure on the intracellular enzyme activities is described. The PAS and Sudan black reactions and the preservation of sideroblasts in fresh and cryopreserved ALL and CLL cells is described. The percentage of T and B cells recovered did not appear to be influenced by the cryopreservation technique and long periods of storage. Although in some cases there was complete dispersion of results between the capability to enter into DNA synthesis for fresh and frozen cells, the cryopreserved blast cells were able to incorporate the tritiated thymidine as well as the fresh cells. The data indicate that frozen leukemia cells exhibit the same cytochemical and immunological properties as do fresh cells. (16 Refs)

### 37. A PRELIMINARY REPORT OF THE INFLUENCE UPON PERIPHERAL BLOOD T-LYMPHOCYTES DURING OPERATIONS UNDER EPIDURAL ANESTHESIA.

**Yu J, Wu G, Yang Y**
**Dept. of Anesthesiology, Affiliated First Hosp., Hubei Medical Coll., Wuham, People's Republic of China**
**Zhonghua Mazuixue Zazhi; 1(1):15-17 1981**

Anesthesia can adversely influence the immune functions of the body causing microorganisms to proliferate and tumors to spread. Prolonged exposure to any common anesthetic can result in decrease of blood leukocytes, especially lymphocytes, thus resulting in an inhibition of immune function. The influence of epidural anesthesia on peripheral blood T-lymphocytes is described for 20 surgical patients (hernia; all males, aged 20-60 yr). Anesthetics used included phenobarbital, atropine, and lidocaine. Using the rates of E-rosette formation as objective criteria for cellular immunity, it was found that they decreased from 55.6% before anesthesia to 41.27, 30 min after anesthesia and to 39.9% 60 min after surgery began. The degree of inhibition was directly proportional to the time of anesthesia. The E-rosetting rates was back to pre-anesthesia levels 151.8%, 24-48 hr after surgery but again dropped slightly 4-5 days after surgery. (16 Refs) (In CHI)

## OTHER RELATED STUDIES

### 38. ULTRASTRUCTURAL, CELL MEMBRANE, AND CYTOGENETIC CHARACTERISTICS OF B-CELL LEUKEMIA, A MURINE MODEL OF CHRONIC LYMPHOCYTIC LEUKEMIA.

**Slavin S, Weiss L, Morecki S, Bassat HB, Leizerowitz R, Gamliel H, Korkesh A, Voss R, Polliack A**
**Dept. Medicine, Immunology Res. Lab., Jerusalem, Israel**
**Cancer Res; 41(10):4162-4166 1981**

A murine model of a spontaneous, transplantable BALB/c B-cell leukemia (BCL1) is described. Extreme leukemia and splenomegaly develop in H-2d-compatible recipients of tumor cells. Tumor cells are medium to large lymphocytes that can be transformed in plasmacytoid cells following in vitro stimulation with lipopolysaccharide. Karyotype analysis of transformed tumor cells reveals 36 chromosomes with several monosomies and 7 marker chromosomes. The ultrastructure of the tumor cells was studied using transmission and scanning electron microscopy. Although the appearance of tumor cells seems normal by morphological criteria, an impaired capping ability was documented using the fluorescein-conjugated con-

canavalin A-binding test. Impaired capping ability was documented before leukemia was overt as early as 1 to 3 days following inoculation of tumor cells. The B-cell leukemia (BCL1) provides a useful murine model for the study of various aspects of human bone marrow-derived malignant disorders. (Author abstract) (28 Refs)

## 39. IMMUNOPATHOLOGY OF NATURAL AND EXPERIMENTAL LYMPHOMAS INDUCED BY WILD MOUSE LEUKEMIA VIRUS.

**Bryant ML, Scott JL, Pal BK, Estes JD, Gardner MB**
**(c/o Gardner) Dept. Pathology, Univ. California Sch. Medicine, Davis, CA, 95616**
**Am J Pathol; 104(3):272-282 1981**

Naturally occurring lymphomas of Lake Casitas (LC) wild mice, and the lymphomas induced by LC murine leukemia virus (MuLV) in Swiss mice from the National Institutes of Health, displayed remarkably similar gross, microscopic, and functional characteristics. They spared the thymus, arose primarily in the splenic red pulp, became leukemic, and were comprised of stem cells lacking classic T- and B-cell markers. Cytoplasmic and surface Ig were undetectable in 34 of 35 spontaneous LC lymphomas and in any of 10 LC MuLV-induced lymphomas in NIH Swiss mice. Assays for Ig secretion, complement (C'3) and Fc receptors, Thy 1.1,2 antigens, Ly 1,2 antigens, and erythroid and myeloid markers were negative on all of the spontaneous and experimental lymphomas. Cell lines were derived from five spontaneous lymphomas of LC mice. Three lines were characterized as null cells, one line as B cells, and one line as macrophages. All cell lines were diploid. The wild mouse spontaneous lymphomas, and lymphomas experimentally induced by LC MuLV in laboratory mice, provide a useful model for childhood acute lymphoblastic leukemia and for study of the early steps of B-lymphocyte differentiation. (Author abstract) (64 Refs)

## 40. THE ANALYSIS OF LYMPHOID SUBPOPULATIONS IN NORMAL AND MALIGNANT TISSUES BY IMMUNOFLUORESCENCE TECHNIQUE.

**Janossy G, Thomas JA, Pizzolo G**
**Dept. Immunology, Royal Free Hosp., Sch. Medicine, Hampstead, London NW3, London**
**J Cancer Res Clin Oncol; 101(1):1-11 1981**

Antibodies labeled with fluorescein isothiocyanate and tetraethylrhodamine isothiocyanate were used to analyze the cellular composition of normal lymphoid tissues and 40 non-Hodgkin's lymphomas by immunofluorescence (IF) in frozen tissue sections. The antisera tested included conventional reagents to immunoglobulin classes, human thymocyte (T cell) and Ia-like antigens, and monoclonal antibodies including the OKT antibodies that react with T-cell subpopulations. The IF technique was found to give an accurate analysis of the normal and malignant cells and to yield information complementary to conventional histology. In normal tissues, the combination of antisera to Ia-like antigens and T lymphoc ytes made it possible to identify reticular cells corresponding to interdigating (ID) cells in peripheral lymphoid tissue. Membrane antigens on ID cells, lamina propria macrophages, and lymphocytes were labeled with a monoclonal antibody to human WBC antigen. Reagent combinations that simultaneously recognized T and B lymphoid cells revealed intriguing variations in the proportion and location of the T cells in B-lymphomas. In some patients, large proportions of T lymphocytes and blasts were clearly seen in close contact with B cells of variable size. Further studies with antibodies to T-cell subsets of inducer and suppressor functions should reveal the clinical significance of these findings. (39 Refs)

## 41. IMMUNOLOGICAL STUDIES ON STOMACH CANCER PATIENTS - WITH SPECIAL EMPHASIS ON EVALUATION OF PARAMETERS AND THOSE SCORING.

**Minami T, Fujimoto S, Takahashi M, Akao T, Kitsukawa Y, Ishigami H, Miyazaki M, Okui K**
**1st Dept. Surgery, Sch. Medicine, Chiba Univ., Chiba City, Japan**
**Nippon Gan Chiryo Gakkai Shi; 16(3):422-432 1981**

The preoperative immunologic status of 100 stomach cancer patients and 18 patients with peptic ulcers or gallstones was compared. Peripheral lymphocyte and T-lymphocyte counts were markedly reduced in patients with inoperable cancer, but B-lymphocyte counts did not differ significantly from those of the controls. Phytohemagglutin (PHA) and purified protein derivative (PPD) skin tests, as well as the PHA-induced lymphoproliferative reaction (PHA-LP), showed no significant difference between the controls and patients with Stages I and II tumors; however, reactions in patients with Stages III and IV tumors diminished gradually according to the clinical stage. Serum immunosuppressive acidic protein (IAP) and T-cell IgG-Fc receptor levels were distinctly higher in Stage IV cancer patients than in the controls. Evaluation of control levels yielded the following abnormal values for the immunologic parameters studied: PHA-LP, stimulation index less than 15; T lymphocytes less than 1,000 cubic mm; T-cell IgG-Fc receptors greater than 9%; serum IAP greater than 500 ug/ml; and reddish erythema less than 20 mm in the PHA skin test and less than 10 mm in the PPD test. In the stomach cancer patients, the range of abnormal values increased with increases in clinical stage. (42 Refs) (In JPN)

## 42. STUDIES ON POSTOPERATIVE CHANGES OF NONSPECIFIC CELL-MEDIATED IMMUNITY IN PATIENTS WITH GASTRIC CANCER.

**Yoshino J**
**Second Dept. Surgery, School Medicine, Mie Univ., Tsu-shi, Mie Prefecture 514, Japan**
**Nippon Geka Gakkai Zasshi; 82(4):355-367 1981**

Postoperative changes of nonspecific cell-mediated immunity were studied in 82 patients with gastric cancer and 17 patients with benign gastric diseases. Among parameters studied preoperatively, lymphocyte count, phytohemagglutinin (PHA) lymphocyte response, and purified protein derivative (P PD) skin test were significantly depressed in the patients with advanced or recurrent carcino ma. No difference of corrected T-cell percent in lymphocytes was found between normal adults and patients with benign gastric disease or gastric cancer. Lymphocyte count, PHA lymphocyte response, neuraminidase-treated sheep RBC (SRBC) rosette formation cell per cent, T-cell count, PPD and PHA skin tests were markedly depressed 2 wk after the operation and recovered to the preoperative value 2 mo after the operation in all the patients, regardless of the nature of the disease, or extension of tumor. Neither postoperative chemotherapy, nor tumor reduction affected these changes. In the long-term observation, however, depression of lymphocyte count, PHA lymphocyte response, and neuraminidase-treated SRBC rosette formation cell percent reflected recurrence or exacerbation of tumor. Depression of neuraminidase-treated SRBC rosette formation cell per cent was particularly useful in precognition of recurrence or exacerbation of tumor. (31 Refs) (In JPN)

## 43. NATURAL AND ACTIVATED CYTOTOXIC LYMPHOCYTES WHICH ACT ON AUTOLOGOUS AND ALLOGENEIC TUMOR CELLS.

**Klein E, Vanky F**
**Dept. Tumor Biology, Karolinska Inst., S-104 01 Stockholm, Sweden**
**Cancer Immunol Immunother; 11(3):183-188 1981**

Evidence for the cytotoxic activity of human blood T lymphocytes is reviewed. T cells are heterogeneous with respect to both activation profile and antigen receptors. Tests of lymphocytes against sensitive cultured cell lines have shown that T cells exert cytotoxic effects on some types of cells without exhibiting antigen recognition. Low natural killer (NK) activity has been demonstrated against freshly harvested tumor cells. NK activity is enhanced by pretreatment of the lymphocytes with interferon (IF). The lytic effect on the tumor cells involves recognition of specific surface antigens. Tests of T cells carrying receptors for histocompatibility antigens against different cell lines have demonstrated T cell specificity. IF does not induce NK activity against autologous tumor cells in most cases. Such activity can sometimes be induced by culturing T cells with allogeneic lymphocytes in mixed lymphocyte cultures (MLC). MLC allow proliferation of anti-autotumor T cells. The proliferation is inhibited by IF. Tumor cells do not show the same sensitivity as cultured cell lines to NK activity not involving antigen recognition. (39 Refs)

## 44. STUDIES OF NONSPECIFIC IMMUNOSUPPRESSION BY PERIPHERAL MONONUCLEAR CELLS FROM CANCER PATIENTS.

**Onodera Y**
**Dept. Internal Medicine, Cancer Res. Inst. Sapporo Medical Coll., Sapporo-shi, Hokkaido, 060, Japan**
**Sapporo Igaku Zasshi; 50(2):113-126 1981**

The immunosuppressive effect of peripheral blood mononuclear cells (PMN) from healthy individuals and patients with advanced cancer was assessed. Mitomycin C-treated normal and cancer PMN were added to the two-way mixed lymphocyte reaction (MLR) to create a three-way MLR. The PMN of 13 of 29 advanced cancer patients, but of none of the healthy subjects or early cancer patients, suppressed the MLR. This suppression was depressed with the depletion of adherent cells from PMN. The culture medium of PMN from advanced cancer patients likewise suppressed the two-way MLR and the activity was also depressed with the removal of adherent cells, although the culture medium of the adherent cells alone showed some activity. The suppressive effect of the culture medium diminished when the medium was preincubated with T cells for 4 hr. To examine the possibility that prostaglandin (PG) is the suppressive material in the culture medium, the patients' PMN were treated with the inhibitor of PG synthetase, indomethacin. The medium from indomethacin-treated PMN from all patients had decreases activity. Radioimmunoassay showed that the PG concentrations in these culture media were increased. Exogenous PGs suppressed the MLR in decreasing order of PG E2, E1 and F2alpha. By receptor assay the receptor sites for PG were found to be on the surface of lymphocytes, particularly T cells. The binding constant and the number of receptors calculated from the Scatchard plot decreased in the order of PG E2, E1 and F2alpha. It was concluded that the suppressive effect of PMN from cancer patients was exerted by a humoral factor, possibly PG, derived from adherent cells, and that the suppressive activity of PG was dependent upon the strength of binding and the number of receptor sites on the surface of the T cells. (53 Refs) (In JPN)

## 45. DESTABILIZATION OF PLASMATIC MEMBRANE AS MECHANISM OF TUMOR CELLS PROTECTION AGAINST IMMUNITY.

**Volkov EI, Chernavskii DS**
**P. N. Lebedev Physical Inst., Moscow, USSR**
**Usp Sovrem Biol; 91(3):419-432 1981**

The phenomenon of progressive tumor growth despite the pronounced humoral and cellular immune response are discussed. Tumor protection against immunity can be explained by weak immunogenicity of tumor antigens or by shedding off the tumor antigens or antigen-antibody complex and blocking the receptors of cytotoxic T lymphocytes. The physical mechanisms of these phenomena can be associated with the loss of stability of tumor cell membrane. Development of the solid-carcass liquid-mosaic model of cell membrane provided an explanation for tumor 'escape'. It was concluded that polyvalent surfactants can stabilize cell membrane and thus enhance the antitumor immunity. (48 Refs) (In RUS)

## 46. IMPAIRMENT OF IN VITRO GENERATION OF CYTOTOXIC OR T SUPPRESSOR LYMPHOCYTES BY FRIEND LEUKEMIA VIRUS INFECTION IN MICE.

**Garaci E, Migliorati G, Jezzi T, Bartocci A, Gioia L, Rinaldi C, Bonmassar E**
**Inst. Microbiology, Univ. Rome, Piazzale Aldo Moro, 00100 Rome, Italy**
**Int J Cancer; 28(3):367-373 1981**

Spleen cells collected from DBA/2 (H-2d) mice inoculated with the polycythemic variant of Friend-Leukemia Virus Complex (FLV-P) were tested for T-dependent immune functions, such as the in vitro generation of cytotoxic T lymphocytes (CTL) and of non-specific T suppressor lymphocytes (STL). CTL were generated against H-2b splenocytes, and STL were obtained following a 5-day lymphocyte culture without stimulator cells. A progressive and severe impairment of the generation of both CLT and STL was found from 2 wk onward after infection, being almost totally abolished 3-4 wk after virus challenge.. Suppressor cells (SC) capable of inhibiting CTL generation were detected in FLV-P bearing mice. Suppressor activity was unaffected by anti-Thy 1.2 serum and complement but was removed following iron-magnet depletion or passage through nylon-wool column. Moreover complete recovery of the competence of CTL generation was attained when FLV-P infected splenocytes were passed through nylon-wool column. It is concluded that FLV-P infection depresses T-dependent cytotoxic and suppressor responses in mice, by the appearance of non-T adherent phagocytic cells, capable of impairing CTL generation in vitro. (Author abstract) (39 Refs)

## 47. CELLULAR IMMUNITY OF PATIENTS AT DIFFERENT STAGES OF ESOPHAGEAL AND GASTRIC TUMORS.

**Horvath OP, Petri I, Kaiser G, Imre J, Petri G**
**I. Sebeszeti Klinika, Szegedi Orvostudomanyi Egyetem, Szeged, Hungary**
**Orv Hetil; 122(26):1567-1572 1981**

The immune reactivity of 17 patients (15 men and 2 women, 30-74 yr old) with tumors of the cardia (13 cases) and esophagus (4 cases) was studied. Radical surgery was performed on five patients without metastases, palliative surgery in six patients, in whom residual tumor was left after surgery or metastases were found, and six patients proved to be inoperable. All inoperable patients and one patient subjected to palliative surgery died within 6 mo, while all patients subjected to radical

surgery and one subjected to palliative surgery were alive 2 yr after surgery. The serum carcinoembryonal antigen (CEA) level was 16 nanog (ng)/ml in 1/5 patients subjected to radical surgery, 5 ng/ml in three, while 5-35 ng/ml was found in 3/6 inoperable patients. The intracutaneous test results were positive in 25% of the patients subjected to radical surgery, 18% in those subjected to palliative surgery, and 2% in the inoperable patients. The results of the E rosette and lymphoblast transformation tests were also reduced significantly compared with the controls. (27 Refs) (In HUN)

## 48. MOBILITY OF SURFACE PROTEINS ON NORMAL RAT MACROPHAGES AND ON A 'MACROPHAGELIKE' RAT TUMOR.

**Woda BA, Yguerabide J, Feldman JD**

**Dept. Anatomic Pathology, City of Hope Natl. Medical Center, Duarte, CA, 91010**

**J Cell Biol; 90(3):705-710 1981**

Peritoneal macrophages endocytosed their histocompatibility antigens (RT1), Fc receptors (FcR), and concanavalin A (Con A) receptors after cross-linking by ligands, but did not cap these membrane proteins. The 323N cell, a 'macrophage like' tumor cell, under identical conditions capped its surface proteins. Experiments measuring fluorescence recovery after photobleaching showed that the mobile fraction of RT1 was significantly greater in 323N cells than in normal peritoneal macrophages. Presumably, the membrane proteins of 323N are not as tethered to the cytoskeleton, or, if so, are in a nexus that is not the same as that which occurs between membrane proteins of normal macrophages and the cytoskeleton. The mobility of RT1 on normal lymphocytes was also different from that of macrophages. These observations suggest that the movement of membrane molecules is determined by cell type and is regulated by the cytoskeleton which varies in structure and function from cell type to cell type. (Author abstract) (18 Refs)

## 49. MACROPHAGES FROM MALIGNANT EFFUSIONS.

**Katz DR**

**ICRF Tumour Immunology Unit, Dept. Zoology, Univ. College London, London WC1E 6BT, England**

**J Pathol; 134(4):279-290 1981**

Cells obtained from 11 patients during paracentesis of serous fluid were examined for macrophage functional attributes and evidence of macrophage malignancy. Clinical diagnosis, later confirmed by autopsy, identified four Hodgkin's disease, two non-Hodgkin's lymphoma, two ovarian carcinoma, one cervical carcinoma, one histiocytic medullary reticulosis, and one cirrhosis. Cells were examined for adherence, surface receptors, and phagocytosis, and by histochemistry and electron microscopy. Macrophages from three Hodgkin's disease patients and from the histiocytic medullary reticulosis case showed striking morphological abnormalities. In the one Hodgkin's disease patient without atypical macrophages, ascites was not due primarily to tumor involvement. Contrary to reports on tissue samples, there was no Hodgkin's disease- related macrophage deficit. Cells from malignant effusions may be a valuable source of information on the histogenesis of tumors which may be of macrophage origin. (18 Refs)

## 50. MACROPHAGE AND T LYMPHOCYTE CONTENT OF TUMORS IN MICE TREATED WITH PROPIONI BACTERIUM.

**Roszkowski K, Roszkowski W, Ko HL, Pulverer G, Jeljaszewicz J**

**Dept. Radiotherapy, Postgraduate Center, Sch. Medicine, Warsaw, Poland**

**Oncology; 38(6):334-339 1981**

Macrophage and T lymphocyte content of sarcoma tumors in mice treated with Propionibacterium granulosum (PG) by different routes was investigated and compared with the effectiveness of the therapy. Two different methods for tumor macrophage detection, the Fc receptor analysis and phagocytic properties, were employed. Indirect fluorescent staining of theta-antigen on lymphocytes was used to evalua te the proportion of tumor T cells. Systemic treatment with PG appeared to be effective if given soon after tumor implantation; however, this route of administration failed to affect the tumor growth if given when the tumor was already advanced. The therapeutic efficiency of intralesional PG injection was almost as effective as early systemic treatment. We obtained evidence indicating that effectiveness of PG therapy was associated with an increase of the macrophage and T cell content of tumors. (Author abstract) (31 Refs)

# AUTHOR INDEX WITH CITATION NUMBERS


Akao T. 41
Albrecht R. 3
Alexander S. 23
Bartocci A. 46
Bassat HB. 38
Baumgartner C. 1
Becker H. 25
Ben-Bassat I. 10
Berchtold W. 1
Bergmann L. 18
Beverley P. 25
Bloom BR. 31
Bonmassar E. 46
Bonnano M. 12
Brok-Simoni F. 10
Bryant ML. 39
Carlow DA. 26
Cazenave PA. 29
Chernavskii DS. 45
Christen Ch. 3
Daar AS. 30
De Biagi M. 36
Delfini C. 36
Delsol G. 8
Dennis JW. 26
Dieckgraefe BK. 28
Dierich MP. 16
Donaghue TP. 26
Duncan WR. 20
Durmuller U. 3
Ebina T. 32
Engelfriet CP. 23
Estes JD. 39
Evsev'eva AI. 35
Fabre JW. 30
Familiades J. 8
Feldman JD. 48
Feller AC. 9
Fujimoto S. 41
Gamliel H. 38
Gamliel H. 4
Garaci E. 46
Gardner MB. 39
Gautier E. 1
Gerdes J. 17
Gioia L. 46
Godde-Salz E. 6
Goldrosen MH. 21
Grote W. 6
Gudat F. 3
Gugler E. 1
Guglielmo P. 12
Gurfel D. 4
Hammerling U. 13
Hasthorpe S. 24
Heitz Ph. 3
Herzenberg LA. 22
Hirashima M. 31
Hirt A. 1
Hitzig WH. 2
Holloway K. 18
Holtzman F. 10
Hoover RG. 28
Horvath OP. 47
Houston LL. 27
Imbach P. 1
Imre J. 47
Iinoshita T. 11
Ishigami H. 41
Ishizaka K. 31
Janossy G. 40
Jeljaszewicz J. 50
Jenkins D. 21
Jezzi T. 46
Joller PW. 2
Jondal M. 14
Jondal M. 15
Juy D. 29
Kadin ME. 7
Kaiser G. 47
Kasahara T. 32
Kasper M. 3
Katz DR. 49
Kerbel RS. 26
Kimura S. 33
Kitsukawa Y. 41
Klein E. 43
Ko HL. 50
Kominek P. 19
Korkesh A. 38
Krey G. 3
Kuhlein E. 8
Lanier LL. 22
Lanzer G. 25
Laurent G. 8
Le Guern C. 29
Ledbetter JA. 22
Leizerowitz R. 38
Leizerowitz R. 4
Lennert K. 6
Lucarelli G. 36
Ludwig Ch. 3
Lynch RG. 28
Maccarrone S. 12
Markowska J. 19
McKenzie IF. 24
Meli C. 12
Merrill JE. 14
Merrill JE. 15
Migliorati G. 46
Minami T. 41
Mitrou PS. 18
Miyata M. 32
Miyazaki M. 41
Morecki S. 38
Morell A. 1
Morioka Y. 32
Mosienko MD. 35
Mulder A. 23
Nesci S. 36
Nordman E. 34
Nowinski RC. 27
Obrecht JP. 3
Okui K. 41
Onodera Y. 44
Oshimi K. 32
Pal BK. 39
Parker JW. 5
Parwaresch MR. 9
Petri G. 47
Petri I. 47
Phillips JT. 20
Pizzolo G. 40
Pluss HJ. 2
Polchi P. 36
Polliack A. 38
Polliack A. 4
Primi D. 29
Pris J. 8
Proia DA. 20
Pulverer G. 50
Raina S. 21
Ramot B. 10
Rigal F. 8
Rinaldi C. 46
Rizzo M. 12
Rogerson J. 24
Roszkowski K. 50
Roszkowski W. 50
Rubartelli A. 13
Russo AJ. 21
Saito M. 32
Sanchez P. 29
Schwarze EW. 6
Scott JL. 39
Sedlmayr P. 25
Simm S. 19
Sitia R. 13
Slavin S. 38
Stein H. 17
Stein H. 6
Stein-Streilein. 20
Streilein JW. 20
Strominger JL. 23
Takahashi K. 32
Takahashi M. 41
Thomas JA. 40
Tilz GP. 25
Toivanen A. 34
Tomaszkiewicz T. 19
Tonz O. 1
Ullberg M. 15
Umansky YuA. 35
Valentini M. 36
Vanky F. 43
Volkov EI. 45
Von dem Borne A. 23
Voss R. 38
Wagner HP. 1
Wakasugi H. 32
Warner NL. 22
Weiss L. 38
Whiteside TL. 11
Woda BA. 48
Wu G. 37
Wyss M. 1
Yang Y. 37
Yguerabide J. 48

Yodoi J. 31
Yoshino J. 42
Yu J. 37
Zerth G. 18
Zurbrugg R. 1
Zybina MA. 35



☆ U.S. GOVERNMENT PRINTING OFFICE: 1982—361-847/110

**U.S. DEPARTMENT OF COMMERCE**
**National Technical Information Service**
5285 Port Royal Road
Springfield, Va. 22161

OFFICIAL BUSINESS

Penalty for Private Use, $300

**PRINTED MATTER**

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF COMMERCE
COM-211

THIRD CLASS
BULK RATE

U.S.MAIL

CB-17

**CANCERGRAMS** are distributed for the International Cancer Research Data Bank (ICRDB) by the National Technical Information Service (NTIS). **CANCERGRAMS** are available from NTIS on a standing order basis at $2 each for North American Continent addressees and $3 each for other addressees. An NTIS deposit account is required. For a list of subject categories or other information, please write to:

Subscription Section
National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161

**NOTICE OF MAILING CHANGE**

☐ Check here if you wish to discontinue receiving this publication.

☐ Check here if your address has changed and you wish to continue receiving this publication. (Be sure to furnish your complete address including zip code.)

Tear off cover with address label still affixed and send to:

Computer Support Center
ICRDB Program
IIT Research Institute
10 West 35th Street
Chicago IL. 60616

CB 17/82/03

NCI/ICRDB/CB17 82/03

PB82-931803

# ICRDB CANCERGRAM

# IMMUNOBIOLOGY AND CANCER

## Identification and Characterization of Immune Cells

SERIES CB17 No. 82/03

MARCH, 1982

This Cancergram is a service of the INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM of the U.S. National Cancer Institute. Every few weeks, an updated Cancergram containing abstracts of selected cancer-related articles recently published in more than 3000 journals, and dealing with the topic indicated by the above title, is sent to researchers working in this area. These researchers are identified on the basis of the description of their current research project that has been submitted to the ICRDB Program, directly or via granting agencies.

This Cancergram is prepared by the Cancer Information Dissemination and Analysis Center (CIDAC) for Virology, Immunology, and Biology. ***If this Cancergram is useful and valuable, please send your comments to the CIDAC address below, since future editions depend on user satisfaction and user needs:***

CIDAC FOR VIROLOGY, IMMUNOLOGY, AND BIOLOGY
SCIENCE INFORMATION SERVICES
FRANKLIN INSTITUTE RESEARCH LABORATORIES
20TH AND RACE STREETS
PHILADELPHIA, PA 19103

NEWARK PUBLIC LIBRARY

APR 13 1982

U. S. GOVT. PUBS.
DEPOSITORY 376

STAY UP TO DATE IN YOUR FIELD. AN AUTOMATIC SDI IN CANCERLIT CAN GIVE YOU A MONTHLY LIST OF NEW ABSTRACTS RETRIEVED BY A CUSTOMIZED SEARCH PROFILE. CONTACT YOUR LIBRARIAN OR THE ICRDB PROGRAM, WESTWOOD BLDG., RM. 10A18, BETHESDA, MD. 20205.

*In this issue:*


- **CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS..... 1-38**
- **DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS..... 39-44**
- **LYMPHOCYTE AND DIFFERENTIATION ANTIGENS..... 45-53**
- **CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION..... 54-60**
- **EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS..... 61-69**
- **OTHER RELATED STUDIES..... 70-90**


**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Public Health Service • National Institutes of Health • National Cancer Institute**

HE 20.3173/2:

## CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS

### 1. MARKER PROFILES OF LEUKEMIA-LYMPHOMA CELL LINES.

Minowada J
Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Haematol Blood Transfus; 26:323-325 1981

Marker profiles (eg, Ia antigen, myelomonocyte antigen, immunoglobulins, Epstein-Barr virus) of 50 leukemia-lymphoma cell lines are presented. The cell lines are divided into three groups: T cell, B cell, or non-T, non-B cells. (4 Refs)

### 2. ESTABLISHMENT AND CHARACTERIZATION OF A CELL LINE DERIVED FROM A PATIENT WITH T-CELL LYMPHOBLASTIC LYMPHOMA. (MEETING ABSTRACT).

Macy ML, Hamburger AW, White CP
Cell Culture Department, American Type Culture Collection, Rockville, MD, 20852
In Vitro; 17(3):225 1981

A new cell line (MARC-I) has been derived from a malignant pleural effusion of a patient with T-cell lymphoblastic lymphoma. The cell line has been in continuous culture for 15 mo and grown in suspension with a doubling x of approx 29 hr. The cells did not require the presence of any exogenous growth factors for their establishment and continued proliferation. The cell line possesses many of the T-cell characteristics of the original cells. Results of histochemical studies on the cell line were similar to the known staining patterns obtained for fresh cells from patients with T-cell neoplasms. The (MARC-I) cells formed rosettes with sheep RBC more efficiently at 4 than 37 C. Approx 10% of the cells exhibited Fc-receptors and 2% of the cells exhibited complement receptors. The cells also expressed HLA antigens and reacted with a monoclonal antibody specific for human T lymphocytes. The following evidence suggests the cells were not derived from normal B lymphocytes present in the pleural effusion. The cells lacked Epstein-Barr nuclear, viral capsid, and early antigens and conditioned medium from the (MARC-I) cells stimulated colony growth of bone marrow cells in soft agar cultures. Moreover, cells from early passages formed colonies in soft agar and produced sc tumors in nude mice. These studies suggest the line was derived from malignant T cells. (no Refs)

### 3. EXPRESSION OF THE OKT MONOCLONAL ANTIBODY DEFINED ANTIGENIC DETERMINANTS IN MALIGNANCY.

Greaves M, Delia D, Sutherland R, Rao J, Verbi W, Kemshead J, Hariri G, Goldstein G, Kung P
Membrane Immunology Lab., Imperial Cancer Res. Fund, London WC2A 3PX, England
Int J Immunopharmacol; 3(3):283-299 1981

Cellular specificity in human leukemia of murine monoclonal antibodies OKT1, 3, 4, 6, 8, 9, 10, 11, and 11A were screened by microscopic and flow cytometric immunofluorescence methods and 125I-binding assays. Tests against malignant T cells showed a correlation between phenotype and clinical diagnosis. T cells from acute lymphoblastic leukemia (T-ALL) cells always showed an immature phenotype. Non-Hodgkin T lymphoma cells showed a cortical thymic phenotype. Both cell types appear to originate from T cell precursors. Cells from chronic T leukemias and cutaneous T lymphomas and leukemias that occur primarily in older adults showed mature T cell phenotypes. OKT11 and OKT11A reacted similarly with sheep E rosettes and appear to react to the same structures. Several T-ALL cell lines were modified in vitro to a more mature phenotype by 12-O-tetradecanoylphorbol 13 acetate or other inducers. This was demonstrated by binding of OKT1, 8, 9, 11, and other antibodies. OKT9 reacted preferentially with T leukemias, but was not T-specific, binding also to other leukemia cells and to other malignant tumor types. Cells induced to mature in vitro lost the OKT9 determinant. OTK9 bound to a receptor that may be a marker for malignancy. OKT10 bound to leukemias and normal bone marrow cells of the myeloid and B cell lineages. OTK6 bound to neuroblastoma cells. (43 Refs)

### 4. SERUM AND SURFACE IMMUNOGLOBULINS IN DIAGNOSIS OF LYMPHOPROLIFERATIVE DISEASES.

Kharchenko MF, Moiseeva VP, Khodzhakulieva AM, Gal'perina IIu, Rybakova LP, Rozanova LM, Ushakova EA, Freidzon VA, Samuskevich IG, Abdulkadyrov KM
Inst. Hematology and Blood Transfusion, Leningrad, USSR
Probl Gematol Pereliv Krovi; 26(8):7-11 1981

To improve the differential diagnosis of lymphoproliferative disorders, serum and surface immunoglobulins (sIg) were determined in 120 patients with chronic lymphoid leukemia (CLL), 12 with blast crisis of CLL, 22 with lymphocytic lymphosarcoma, and 5 with with lymphoblastic lymphosarcoma. Significant increase of a number of sIg-positive lymphocytes carrying predominantly IgM was recorded in a majority of CLL patients. The density of sIg in the patients with non-Hodgkin's lymphomas was significantly greater than that in the CLL patients. (13 Refs) (In RUS)

### 5. CLASSIFICATION OF HUMAN LEUKEMIA BY MEMBRANE ANTIGEN ANALYSIS WITH XENOANTISERA.

Metzgar RS, Dowell BL, Lachman LB, Jones NH, George FW
Dept. Microbiology and Immunology, Duke Univ. Medical Center, Durham, NC, 27710
Cancer Res; 41(11,part2):4781-4785 1981

Rabbit and monkey antisera after appropriate absorption were rendered specific for normal or leukemic lymphoid- and myeloid-associated antigens. Antisera defining a common peripheral blood T-cell antigen, a thymus leukemia antigen, HLA-DR or Ia-like antigen (CALLA) common acute lymphoblastic leukemia antigen, and a myeloid-monocyte (M) antigen were used in a microcytotoxicity assay to classify leukemic cells from 30 patients in a double blind study. The antisera to the M antigen reacted with adherent peripheral blood cells and polymorphonuclear leukocytes and failed to react with nonadherent mononuclear cells and enriched T-cells and chronic lymphocytic leukemia cells. The M antisera also reacted with U937, a monocytic-type cell line, and with HL60, a promyelocytic-type cell line, but failed to react with T and B lymphoblastoid cell lines. The specificities of the other antisera have been described in previous reports. Cells from three of the patients could not be phenotyped by microcytotoxicity testing. Cells from 25 patients had a consensus morphological or histochemical diagnosis of either acute lymphoblastic leukemia or acute nonlymphocytic leukemia. The serological classification of these patients using the five types of antisera listed above were consistent with the consensus diagnosis. In addition, the lymphoid cancers were further sub-classified as to T-, B-, or thymus antigen types. There was no consensus lymphoid versus myeloid diagnosis on cells from two patients. The serological classification in both cases favored a diagnosis of mye-

loid rather than lymphoid leukemia. (Author abstract) (20 Refs)

## 6. A CLINICAL PERSPECTIVE ON CELL MARKERS IN ACUTE LYMPHOCYTIC LEUKEMIA.

**Bowman WP, Melvin SL, Aur RJ, Mauer AM**
**Div. Hematology-Oncology, St. Jude Children's Res. Hosp., Memphis, TN, 38101**
**Cancer Res; 41(11,part2):4794-4801 1981**

Two hundred consecutive new patients, with acute lymphocytic leukemia (ALL) have been studied with a battery of five cell marker assays to determine if a classification system with prognostic significance can be developed; 182 have been classified among four groups as follows: 33 T-cell, 3 B-cell, 126 common, and 20 undifferentiated ALLs. Patients with T-cell disease are likely to have unfavorable clinical prognostic features and a poor response to therapy. Rare patients with B-cell disease are closely related clinically to non-Hodgkin's lymphoma. Those with common ALL infrequently have unfavorable clinical features and have a superior outcome to that of T-cell patients. Children with undifferentiated markers seem to respond less well to treatment than do those with common ALL, yet may not be identifiable as poor risk by clinical features. What remains to be resolved with further observation is whether these marker patterns are more reliable indicators of prognosis than the usual clinical determinants predisposing to treatment failure (high WBC count, mediastinal mass, and CNS disease). At the present time, it appears that in the absence of poor-risk clinical prognostic features, patients with common ALL are more likely to have lasting remissions than those with RBC-rosette-positive T-cell disease or those with ALL that is undifferentiated by markers. (Author abstract) (9 Refs)

## 7. ANALYSIS OF THE CLINICAL AND BIOLOGICAL SIGNIFICANCE OF LYMPHOID PHENOTYPES IN ACUTE LEUKEMIA.

**Greaves MF**
**Membrane Immunology Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England**
**Cancer Res; 41(11,part2):4752-4766 1981**

Analysis of leukemia cell phenotypes using cell surface antigens and various enzymes indicates that acute lymphoblastic leukemia (ALL) is a biologically heterogeneous disease consisting of four major subclasses with additional subsets existing within these subclasses. These different types of ALL appear to reflect sequential stages of early lymphocyte ontogeny. There is a strong association between cell phenotype and first remission duration in ALL (p trend less than 0.0001) and an equally strong correlation between remission duration and WBC count at presentation. If common ALL and thymic ALL ( T-ALL) are compared after adjustment of WBC counts, then the prognostic differences between these two major subclasses almost disappear ($p = 0.38$). It is suggested, therefore, that an immunological (and enzymatic) phenotype of ALL subclasses may not be an independent correlate of prognosis but nevertheless is linked to other differentiation-linked features, especially growth rate and sites of clonal expansion (eg, marrow versus thymus), which critically influence the size of the clonogenic leukemic population and its associated evolutionary status with respect to drug-resistant mutants at the time of diagnosis and introduction of therapy. An extensive library of monoclonal antibodies has been used to further define the phenotypic heterogeneity of T- and non-T ALL. Several of the antigenic structures identified by these monoclonal antibodies have been isolated and characterized. T-ALL can be dissected into several subsets - corresponding to stages of intrathymic differentiation. Non-T ALL (null-ALL, common ALL, and B-ALL) all have a phenotype indicative of B-lineage affiliation indicating that 'non-T, non-B' ALL may originate from B-cell precursors in bone marrow. A cell type is identified in normal bone marrow which has the same identical monoclonal antibody-defined phenotype as common ALL and may provide the target cell for this disease. (Author abstract) (94 Refs)

## 8. SOUTHWEST ONCOLOGY GROUP EXPERIENCE WITH IMMUNOLOGICAL PHENOTYPING IN ACUTE LYMPHOCYTIC LEUKEMIA OF CHILDHOOD.

**Pullen DJ, Falletta JM, Crist WM, Vogler LB, Dowell B, Humphrey GB, Blackstock R, Van Eys J, Cooper MD, Metzgar RS, Meydrech EF**
**Operations Office, Southwest Oncology Group, 3500 Rainbow Blvd., Suite 100, Kansas city, KS, 66103**
**Cancer Res; 41(11,part2):4802-4809 1981**

The Pediatric Division of the Southwest Oncology Group is attempting to define subgroups of acute lymphoblastic leukemia (ALL) by laboratory delineation of marrow lymphoblast characteristics at diagnosis. Immunological subclassification studies include erythrocyte-forming rosette (E-rosette), C3 receptor, Fc receptor, surface Ig (Sig) and cytoplasmic Ig (CIg) determinations, as well as peripheral T (PT), thymocyte, Ia, and common ALL membrane antigen testing. Four subgroups of ALL have thus far been defined: null (SIg-, CIg,-, PT-); pre-B (SIg-, CIg+, PT-); B-cell (SIg+, CIg-, PT-); and T-cell (SIg-, CIg-, PT+). A group of 118 patients have had complete testing, and an additional 121 patients have had partial testing. Thirty-five patients with pre-B ALL and 27 patients with T-cell ALL have thus far been studied. Pre-B and null types of ALL appear closely related in multiple subclassification parameters (age, sex, physical findings, WBC count, and lymphoblast Ia and common ALL antigen positivity). Pre-B ALL patients treated with the same treatment regimens as were null ALL patients appear to have shorter durations of complete remission, although the difference has not yet reached statistical significance. Results suggest that the male predominance and older age distribution previously recognized for E-rosette-positive T-cell leukemia can also be expected in the E-rosette-intermediate and E-rosette-negative T-cell ALL subsets, although statistically higher WBC counts at diagnosis are seen in the E-rosette-positive subset. Mediastinal mass at diagnosis is most likely in the patient with E-rosette-positive, thymocyte antigen-positive lymphoblasts. The E-rosette intermediate and E-rosette negative, as well as the E-rosette positive, T-cell ALL subsets appear to constitute poor prognosis categories. Correlation with treatment results is preliminary in all groups but suggests that stratification of ALL at diagnosis according to several immunological subgroupings may prove helpful in planning therapy. (Author abstract) (32 Refs)

## 9. CYTOCHEMICAL MARKERS OF DIFFERENTIATION IN ACUTE LEUKEMIA.

**Catovsky D, De Salvo Cardullo L, O'Brien M, Morilla R, Costello C, Galton D, Ganeshaguru K, Hoffbrand V**
**MRC Leukaemia Unit., Royal Postgraduate Medical Sch., Ducane Road, London W12 OHS, England**
**Cancer Res; 41(11,part2):4824-4832 1981**

Material from 110 adult patients with acute myeloid leukemia, acute lymphoblastic leukemia, and chronic granulocytic leukemia (CGL) in blast crisis (BC) was studied by light microscopy (LM) and transmission electron microscopy cytochemistry in order to examine the sensitivity of the tests used to

define myeloid differentiation. Granulocytic differentiation was best visualized by the myeloperoxidase (MPO) reaction. By LM, the Hanker method using 3,3'-diaminobenzidine at pH 7.6 was the most sensitive in demonstrating MPO and the presence of phi bodies in most acute myeloid leukemias and some CGLs in 'myeloid' BC. Phi bodies were more numerous when the reaction was carried out at pH 9.7, suggesting that they originate from catalase-containing microperoxisomes. MPO at transmission electron microscope level (with 3,3'-diaminobenzidine) was more sensitive than the LM techniques because it demonstrated myeloblasts with few positive granules and reaction product in the endoplasmic reticulum. The platelet-peroxidase technique of Breton-Gorius, using a higher concentration of 3,3'-diaminobenzidine and unfixed material, was of even greater sensitivity for the study of myeloid precursors and allowed the identification of megakaryoblasts in CGL in BC. Monocytic differentiation was best recognized by LM using an esterase method (naphthol AS-acetate or alpha-naphthyl acetate) and the acid phosphatase reaction. By transmission electron microscopy, the acid phosphatase reaction was positive in small electron-dense granules which are MPO negative and appear to be characteristic of the early maturation stages of monoblasts. The techniques desc ribed were of value in the classification of CGL in BC and demonstrating the myeloid component in 8 of 56 (14%) acute myeloid leukemia cases which were positive with the enzyme terminal transferase. Five of the latter were 'pure' myeloid cell proliferations, and three others were 'mixtures' of lymphoblasts and myeloblasts (or monoblasts), but with lymphoid cells predominating in two of them. (Author abstract) (31 Refs)

## 10. USE OF MONOCLONAL ANTIBODIES AS DIAGNOSTIC AND THERAPEUTIC REAGENTS IN ACUTE LYMPHOBLASTIC LEUKEMIA.

**Ritz J, Pesando JM, Notis-McConarty J, Clavell LA, Sallan SE, Schlossman SF**
**Div. Tumor Immunology, Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115**
**Cancer Res; 41(11,part2):4771-4775 1981**

A monoclonal antibody specific for a common acute lymphoblastic leukemia (ALL) antigen has been generated and characterized. This antibody (J-5) is reactive with leukemic cells from most patients with non-T-cell ALL and some patients with chronic myelocytic leukemia in blast crisis. J-5 antibody is not reactive with leukemic cells from patients with either T-cell ALL, chronic lymphocytic leukemia, acute myeloblastic leukemia, or stable-phase chronic myelocytic leukemia. In addition to diagnostic applications, anti-common ALL antigen monoclonal antibody has been used to study the effect of specific serotherapy in the treatment of ALL. In the first patient with ALL treated with J-5 antibody, a 90% reduction in circulating lymphoblasts occurred within 1 hr of starting antibody infusion. Despite continued serotherapy, however, lymphoblasts persisted in peripheral blood and bone marrow. Analysis of cell surface markers during serotherapy suggested that resistance to antibody-mediated lysis in vivo may have been due to antigenic modulation of leukemic cells in response to J-5 monoclonal antibody. (Author abstract) (27 Refs)

## 11. CELL SURFACE MARKERS AND KINETIC FEATURES IN ACUTE LYMPHOBLASTIC LEUKAEMIA.

**Caligaris Cappio F, Novarino A, Matera L, Gavosto F**
**Cattedra de Patologia Medica I., C.so Polonia 14, 10126 Torino, Italy**
**Haematologica (Pavia); 66(4):419-425 1981**

The labelling index (LI) of cell surface antigen SM+ and SM- blast cells from 15 patients (11 children: 7 males, 4 females; 2-11 yr old; 4 adults: 3 men, 1 woman; 23-37 yr old) with acute lymphoblastic leukemia (ALL) and from 1 patient with chronic myelocytic leukemia (CML) in lymphoid-like blast crisis was examined. In the four cases of SM+ ALL studied (3 T-cell ALL and 1 B-cell ALL), the LI of bone marrow blasts was 9.47 +-3.90 (range 6.1-16.7) compared with 1.38 +-1.19 (range 0.6-4.0, p less than 0.01) in the 11 cases of ALL without conventional T and B markers. Cells from the patient in a lymphoid-like blast crisis of CML had a bone marrow LI of 5.7. Upon combined immunofluorescent and autoradiographic anal ysis of bone marrow blasts, SM+ blast always displayed LI values significantly higher than SM- blasts. The data indicated that in acute leukemia blast cell populations, SM+ and SM- blasts have different LI. The relationship of this phenomenon to the problems of blast proliferation and differentiation are discussed. (16 Refs)

## 12. IMMUNOLOGICAL DEFINITION OF LEUKEMIC CELL SURFACE PHENOTYPES.

**Melvin SL**
**Div. Immunology, St. Jude Children's Res. Hosp., Memphis, TN, 38101**
**Cancer Res; 41(11,part2):4790-4793 1981**

Immunological phenotyping of blasts from over 200 children with acute lymphocytic leukemia (ALL) reveals both interpatient differences and phenotypic heterogeneity in the blast population from individual patients. A battery of five independent lymphocyte differentiation markers, RBC-forming rosettes, T-cell antigens, Ia-like antigens, the common ALL antigen, and surface Ig, permit classification of all ALL specimens into four major marker groups. These are common, T-cell, B-cell, and undifferentiated ALL. Heterogeneity in the marker phenotypes within each of the major groups is observed. Within individual RBC receptor-positive ALL specimens, phenotypic heterogeneity in the blast population is demonstrated. Sequential determinations of the blast phenotype during periods of active disease reveal a second example of intrapatient blast cell heterogeneity. Differences in phenotype of the dominant blast populations present prior to treatment and at relapse are observed in sequential studies of individual patients. These shifts in phenotype are nonrandom. They result most frequently from losses in single differentiation markers. A unifying hypothesis which explains these observations of phenotypic heterogeneity is that ALL blasts manifest limited lymphoid-like differentiation. (Author abstract) (8 Refs)

## 13. COMPARATIVE ANTIGENIC PHENOTYPES OF NORMAL AND LEUKEMIC HEMOPOIETIC PRECURSOR CELLS ANALYSED WITH A 'LIBRARY' OF MONOCLONAL ANTIBODIES.

**Greaves MF, Robinson JB, Delia D, Ritz J, Schlossman S, Sieff C, Goldstein G, Kung P, Bollum FJ, Edwards PA**
**Imperial Cancer Res. Fund Lab., P.O. Box 123, Lincoln's Inn Fields, London WC2A 3PX, England**
**Haematol Blood Transfus; 26:296-304 1981**

Antigenic phenotypes of normal and leukemic hemopoietic precursor cells were compared using a surface protein associated with common acute lymphoblastic leukemia (cALL), the gp 28/33 Ia-like or HLA-DR antigens, and a number of monoclonal antibodies. About 33% of cALL cells have a pre-B cell phenotype. Most have no mature T or B cell markers, and presumably represent hemopoietic precursor cells in maturation arrest. Leukemic cells also have the nuclear enzyme TdT. The cALL antigen and TdT have been found in a small number of

normal lymphoid cells in bone marrow. These cells appear to have the same surface pheno type as cALL cells, indicating that cALL cells may not have leukemia-specific surface markers. The cellular expression of HLA-DR antigen in leukemic cells is matched by its expression on hemopoietic progenitor cells of myeloid and erythroid lineages. Surface phenotype of leukemic cells appears to reflect the stage of maturation at which they were arrested, rather than a leukemia-specific form. How closely leukemic phenotype corresponds to normal developmental phenotype is, however, uncertain. (59 Refs)

## 14. NEW ANTIGENIC DETERMINANT COMMON TO HUMAN THYMUS LEUKAEMIA-ASSOCIATED ANTIGENS AND COMMON ACUTE LYMPHOBLASTIC LEUKAEMIA ANTIGEN.

**Negoro S, Yoshizaki K, Henderson ES, Seon BK**
**(c/o Seon) Dept. Immunology Res., Roswell Park Memorial Inst., Buffalo, NY, 14263**
**Clin Exp Immunol; 45(3):487-495 1981**

In the present paper we demonstrate that there is an antigenic determinant common to two different types of human leukemia-associated antigens, ie human thymus leukemia-associated (HTL) antigens and common acute lymphoblastic leukemia (cALL) antigen. In addition, there are distinct antigenic determinants which are unique to the HTL antigens or to the cALL antigen. The new, common antigenic determinant will be useful as a new differentiation marker of human hematopoietic cells as well as a new leukemia-associated marker. In the present study, we used several different anti-human leukemia antisera which include those prepared by immunizing rabbits (Numbers 7549 and 7550) with purified HTL antigens. The antisera 7549 and 7550, without any absorption, showed strong specificity as well as strong antibody activity toward leukemia cells. These are the first anti-human leukemia antisera, except for the monoclonal hybridoma antibodies, that show good specificity for leukemia cells without prior absorption. (Author abstract) (33 Refs)

## 15. CLASSIFICATION OF ACUTE LEUKEMIAS.

**Imbert M, D'Agay MF, Andre C, Sultan C**
**Laboratoire d'Hematologie-Immunologie, Hopital Henri-Mondor, 51, avenue de Lattre-de-Tassigny, 94010 Creteil, France**
**Ann Biol Clin (Paris); 39(4):155-164 1981**

Morphological, electron microscopic, immunologic, and chromosomal classifications of acute leukemias are discussed. Morphological classification is based on blood and bone marrow smears and on certain simple cytochemical reactions. According to this schema leukemia can be classified as acute lymphoblastic (L1, L2, or L3, Burkitt's type) and acute myeloblastic (without or with maturation, hypergranular promyelocytic, myelomonocytic, acute monocytic, and erythroleukemia, M1-6, respectively). Electron microscopic analysis permits the analysis of the fine structure of Auer bodies and allows the recognition of the myeloid (myeloblastic or megakaryocytic) nature of certain leukemias classified as lymphoblastic or undifferentiated on the basis of cytological or cytochemical findings. Immunologic study, using membrane markers, provides useful information for the classification of lymphoblastic leukemias as T-cell, B-cell, and non-T, non-B-cell leukemias. Biochemical tests utilizing lysozyme and terminal-deoxynucleotidyltransferase measurements are described. Karyotypic anomalies can also be associated with various forms of acute lymphoblastic or myeloblastic leukemia. (57 Refs) (In FRE)

## 16. CHARACTERISTIC FEATURES OF ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN WITH 0-CELLS IN THE BONE MARROW AND PREDOMINANCE OF T- OR B-CELLS IN THE PERIPHERAL BLOOD.

**Lenskaia RV, Samochatova EV, Rumiantsev AG, Izotova TA**
**No affiliation given**
**Probl Gematol Pereliv Krovi; 26(7):20-24 1981**

Different markers of the leukemic cells in the bone marrow and the peripheral blood were reported in 11 children (5 boys, 6 girls, aged 4 to 13 yr) with acute lymphoblastic leukemia (ALL). Examination of the bone marrow showed total metaplasia with lymphoid leukemic cells; greater than 80% of leukemic cells could be identified as null-lymphocytes. Analysis of the lymphoid cells in the peripheral blood showed predominance of T-lymphocytes in 10 patients and predominance of B-lymphocytes in 1. Chemotherapy (prednisone in combination with vincristine) induced stable and prolonged remission in 10/11 patients. (8 Refs) (In RUS)

## 17. DETECTION OF ERYTHROBLASTIC ANTIGEN ON THE BLAST SURFACE IN CERTAIN VARIANTS OF ACUTE LEUKEMIA.

**Idel'son LI, Pivnik AV, Ievleva ES, Ter-Grigorov VS, Graf IA, Tikhonova LIu**
**Dept. Hematology, Central Inst. Advanced Training for Physicians, Moscow, USSR**
**Probl Gematol Pereliv Krovi; 26(8):16-21 1981**

To evaluate whether the monospecific antibodies against the interspecies erythroblastic antigen (EA) can be used for detection of nondifferentiated erythrokaryocyte precursors, blast cells from four patients with different variants of acute leukemia were studied in immunofluorescence reaction. One patient with acute erythromyelosis showed specific fluorescence of erythrokaryocytes; progressive differentiation of erythromyelosis into acute myeloblastic leukemia was associated with the decrease of erythrokaryocyte count and simultaneous disappearance of surface EA. Another three patients developed acute leukemia after a stage of complete inhibition of erythropoietic stem cells; specific fluorescence was associated with blast cells rather than with the erythrokaryocytes. The decrease of the number of fluorescent cells in these patients was not correlated with the decrease of the number of blast cells. (21 Refs) (In RUS)

## 18. USE OF MONOCLONAL ANTIBODIES, MORPHOLOGY, AND CYTOCHEMISTRY TO PROBE THE CELLULAR HETEROGENEITY OF ACUTE LEUKEMIA AND LYMPHOMA.

**LeBien TW, McKenna RW, Abramson CS, Gajl-Peczalska KJ, Nesbit ME, Coccia PF, Blo omfield CD, Brunning RD, Kersey JH**
**Dept. Lab. Medicine and Pathoogy, Univ. Minnesota, Box 609 Mayo, Minneapolis, MN, 55455**
**Cancer Res; 41(11,part2):4776-4780 1981**

A combined immunological, morphological, and cytochemical approach to the study of malignant cells in patients with acute leukemia and lymphoma is presented. Newly produced monoclonal antibodies that bind to antigens of human mononuclear cells (TA-1), or B-lymphocytes (BA-1) were used to study malignant cells from patients with acute lymphoblastic leukemia (ALL), acute myelocytic leukemia, acute myelomonocytic leukemia, and chronic lymphocytic leukemia. Results in lymphoid leukemia-lymphoma patients were compared with other immunological markers and indicate that the major groups of ALL and childhood non-Hodgkin's lymphoma are

T-ALL, pre T-ALL, pre-B-ALL, and non-T, non-B-ALL. In addition, each major group had multiple phenotypes when analyzed with seven immunological markers including the RBC rosette receptor, surface Ig, cytoplasmic Ig M, the early lymphocyte-acute lymphoblastic leukemia antigen, monoclonal antibody TA-1, monoclonal antibody BA-1, and a monoclonal antibody against HLA-Dr. While immunological heterogeneity was demonstrable within each group, distinct biological behavior was observed, with T-ALL and B-ALL generally presenting as 'lymphomas' and the others presenting as 'leukemias.' Morphological analysis using the French-American-British classification provided independent information in the definition of groups with differing clinical behavior. Cytochemical analyses demonstrated focal paranuclear staining of leukemia cells with acid phosphatase in 73% of T-ALLs and 6% of non-T, non-B-ALLs. (Author abstract) (32 Refs)

## 19. PURINE PATHWAY ENZYME ABNORMALITIES IN ACUTE LYMPHOBLASTIC LEUKEMIA.

**Poplack DG, Blatt J, Reaman G**

**Pediatric Oncology Branch, NCI, NIH, Building 10, 3B03, Bethesda, MD, 20205**

**Cancer Res; 41(11,part2):4821-4823 1981**

The status of three purine pathway enzymes, adenosine deaminase, 5'-nucleotidase, and purine nucleoside phosphorylase, was evaluated in the leukemic cells of patients with acute lymphoblastic leukemia and correlated with routine immunological cell surface markers. A distinct pattern of enzyme activity was noted in T-lymphoblasts which have significantly higher adenosine deaminase activity (p less than 0.02) and lower 5'-nucleotidase (p less than 0.001) and purine nucleoside phosphorylase (p less than 0.01) activities than do non-T, non-B lymphoblasts. This enzyme pattern is similar to that observed in normal human thymocytes but is not shared by the mature, normal T-lymphocytes of peripheral blood, suggesting that it may reflect the differentiation status of malignant T-lymphoblasts. These findings, which confirm the biochemical heterogeneity of acute lymphoblastic leukemia, may provide an avenue for selecti ve chemotherapy of this disease. (Author abstract) (19 Refs)

## 20. DEFINITION OF THE HIGH-RISK ACUTE LYMPHOBLASTIC LEUKEMIA PATIENT BY IMMUNOLOGICAL PHENOTYPING WITH MONOCLONAL ANTIBODIES.

**Zipf TF, Fox RI, Dilley J, Levy R**

**(c/o Levy) Dept. Medicine/Oncology, Stanford Univ., Stanford, CA, 94305**

**Cancer Res; 41(11,part2):4786-4789 1981**

An accurate method of classification of the surface membrane characteristics of blast cells from patients with acute lymphoblastic leukemia would allow a more definitive study of the nature of this disease. Monoclonal antibodies have been produced to the surface antigens of leukemic blasts from a patient with high-risk acute lymphoblastic leukemia. Two antibodies of interest were obtained from this immunization. These two, in combination with a monoclonal antibody with anti-Ia specificity, have been used to obtain surface phenotypes for patients with childhood acute lymphoblastic leukemia. Preliminary results indicate that the definition of a high-risk group, using these antibodies, is possible. (Author abstract) (16 Refs)

## 21. NEW DATA ON CHRONIC LYMPHOCYTIC LEUKEMIA.

**Rupniewska ZM, Dmoszynska-Giannopoulou A**

**Klinika Hematologii, Instytut Chorob Wewnecrznych Akademii Medycznej, ul. Jaczewskiego 8, 20-950 Lublin, Poland**

**Acta Haematol Pol; 12(2):107-112 1981**

Recent studies on chronic lymphocytic leukemia (CLL) are reviewed. More than 75% of the patients are over 60 yr old, and CLL affects twice as many men as women. The serum immunoglobulin is often polyclonal, and there is hypogammaglobulinemia in the majority of the cases. The leukemia cells carry Fc IgG receptor, receptor for complement (RC), and receptor for mouse erythrocytes. About 11% of all cases are characterized by the presence of two subtypes of complement receptor (1 RC and 2 RC). T-cell markers occur in 1-2.9% of all cases. (59 Refs) (In POL)

## 22. ON THE BIOLOGY AND IMMUNOLOGY OF HODGKIN'S DISEASE.

**Kaplan HS**

**Dept. Radiology, Cancer Biology Res. Lab., Stanford Univ. Medical Sch., Stanford, CA, 94305**

**Haematol Blood Transfus; 26:11-23 1981**

Biological and immunological characteristics of Hodgkin's diseases (HD) are presented. Giant cells of HD satisfy two of the most fundamental attributes of neoplasia: aneuploidy and clonal derivation. Cell culture and immunofluorescence studies have provided information concerning the origin and nature of the HD giant cells. Their capacity for sustained proliferation in vitro, aneuploidy, and heterotransplantability establishes their neoplastic character, whereas the cell marker studies, phagocytic activity, positive staining reactions for nonspecific esterase, and capacity to excrete lysozyme strongly suggest that they are derived from the macrophage or other closely related cells of the mononuclear ph agocyte system rather than from the lymphocyte. The natural history and mode of spread of HD is discussed. Study results indicating that virtually all HD patients, including those with localized involvement, suffer from a selective, often subtle, impairment of cell-mediated immunity are presented. In vivo, this deficit is expressed by an increased susceptibility to certain types of bacterial, fungal, and viral infections and by decreased capacity for delayed hypersensitivity reactions to recall antigens or chemical allergens. A spectrum of in vitro test results are also impaired. These alterations may be due to functional alterations of T-lymphocytes rather than to quantitative depletion of either T- or B-lymphocytes. Human inhibitors in the sera of HD patients and suppressor cell effects have also been implicated. (37 Refs)

## 23. MONOCLONAL ANTIBODY AGAINST A BURKITT LYMPHOMA-ASSOCIATED ANTIGEN.

**Wiels J, Fellous M, Tursz T**

**Laboratoire d'Immunologie Clinique, Institut Gustave-Roussy, 94800 Villejuif, France**

**Proc Natl Acad Sci USA; 78(10):6485-6488 1981**

A monoclonal antibody, referred to as 38.13, was obtained by fusing murine myeloma cells with Lewis rat splenocytes sensitized with Daudi cells (human Burkitt lymphoma containing Epstein-Barr virus genome but lacking HLA-A, -B, and -C and beta2-microglobulin molecules at the cell surface). 38.13 antibody was demonstrated to be a rat IgM. By complement-dependent microcytotoxicity and indirect immunofluorescence assays, 38.13 antibody was shown to react specifically with cells derived from Burkitt tumors, including both Epstein-Barr

virus genome-carrying and Epstein-Barr virus-negative Burkitt lymphoma. By contrast, Epstein-Barr virus-containing lymphoblastoid cell lines derived from normal B lymphocytes were not recognized by 38.13 antibody. Fresh malignant cells from patients affected with various lymphoproliferative disorders were negative, except 4/8 having abdominal Burkitt-like lymphomas. Normal lymphocytes from peripheral blood, spleen, lymph node, tonsil, and bone marrow and mitogen (phytohemagglutinin, pokeweed mitogen, and concanavalin A)-activated blasts were also negative. Thus, 38.13 antibody apparently recognized a Burkitt-associated antigen that is not related to Epstein-Barr virus. The pattern of reactivity of 38.13 antibody with various Burkitt lymphoma cells appeared quite heterogenous and some Burkitt cells were consistently negative. 38.13 antibody thus defines a subset of Burkitt lymphomas. (Author abstract) (18 Refs)

## 24. PREDICTIVE ABILITY OF LUKES-COLLINS CLASSIFICATION FOR IMMUNOLOGIC PHENOTYPES OF CHILDHOOD NON-HODGKIN LYMPHOMA: AN INSTITUTIONAL SERIES AND LITERATURE REVIEW.

**Crist WM, Kelly DR, Ragab AH, Roper M, Dearth JC, Castleberry RP, Flint A**
**Div. Hematology/Oncology, Children's Hosp., 1601 6th Ave. South, Birmingham, AL, 35233**
**Cancer; 48(9):2070-2075 1981**

Tissues from 22 children with non-Hodgkin lymphoma (NHL) were studied pathologically and immunologically. Most children were noted to have marked (B- or T-cell) neoplasms and the Lukes-Collins classification was predictive of immunologic phenotype in cases where markers were presented. Our series and a review of the literature demonstrates that most abdominal NHL are B-cell in origin and are often small noncleaved follicular center cell lymphoma (Burkitt type). Most mediastinal primary lesions are T-cell in origin and of convoluted cell morphology. a few neoplasms (often peripheral nodal) lack the characteristic surface Ig or RBC rosetting properties of B- or T-cell lesions, respectively. Frequently marrow and CNS involvement are observed in T-cell lymphomas and are not infrequent in B cell neoplasms. Shared immunologic and clinical features between the B- or T-cell lymphomas and their leukemic counterparts support the concept that they often differ only in the stage of disease progression. (Author abstract) (22 Refs)

## 25. IMMUNOHISTOLOGICAL DETERMINATION OF CELL SURFACE STRUCTURES IN HUMAN LYMPHOMAS AND ITS DIFFERENTIAL DIAGNOSTIC VALUE (MEETING ABSTRACT).

**Stein H**
**Institute of Pathology, University of Kiel, 2300 Kiel, W. Germany**
**Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland. The Congress 92 pp., 1981.**

The goal of the study was to improve the characterization of normal and malignant lymphoid subpopulations by immunostaining frozen and paraffin sections of malignant non-Hodgkin's lymphomas for surface (S) and cytoplasmic (C) antigens. Immunostaining was performed with the immunoperoxidase method using polyclonal antisera and monoclonal antibodies (MCA). Cells of B-type chronic lymphocytic leukemia (B-CLL) showed positive staining for SIgM and SIgD with only one light chain, B-cell specific antigens Leu1, HLA-DR, and C3 receptors. Hairy cell leukemia cells reacted for SIg with one light chain and for HLA-DR, but not for Tu1, Leu1, or C3 receptors. Follicular centroblastic-centrocytic lymphoma (CB-CC) was characterized by the expression of SIg with one light chain, Tu1, C3RTo15, HLA-DR, and C3 receptors and the absence of Leu1 and SIgD. Follicular CB-CC was found to have a specific feature: follicle-like collections of dendritic reticulum cells (DRC) amog the neoplastic B cells, as revealed by staining with the MCA CR4/23. All the lymphomas with a diffuse growth pattern showed no, or only a few solitary DRC among the neoplastic cells. SIg was detectable in more than 80% and CIg in 70% of the cases of immunoblastic lymphoma. Using various T cell-specific reagents (OKT3, 4, 8, 11, Tu12, 13, 14, 33, HTA-1), the T-cell neoplasms appeared to be highly heterogeneous. (no Refs)

## 26. CELLULAR MARKERS IN MALIGNANT LYMPHOMAS AND THEIR CLINICAL IMPORTANCE.

**Morell A, Hirt A**
**Institut fur klinisch-experimentelle Tumorforschung, Universitat Bern, CH-3004 Bern, Switzerland**
**Ther Umsch; 38(9):854-861 1981**

Recent studies of cellular markers and their clinical significance in malignant lymphoma are reviewed. The study of immunological and biochemical markers shows that the lymphoid cells of non-Hodgkin's lymphomas (NHL) represent subpopulations of B or T cells at different stages of differentiation. Current evidence indicates that the neoplastic cells of follicular lymphoma are all B lymphocytes. Diffuse lymphomas may be derived from the B cell line or, less frequently, from T cells. About 1/3 of all NHL lack surface and cytoplasmic markers and are categorized as 'null' cell lymphomas. It is unknown, if the Sternberg-Reed cells in Hodgkin's disease derive from the monocyte-macrophage series or from B cells. The prognostic significance of marker analysis in malignant lymphoma has not yet been established clearly, but abdominal B-cell lymphomas of childhood have a definitely poor prognosis and some studies suggest that 'null' cell lymphomas in adults have a considerably worse prognosis than comparable B-cell lymphomas. (14 Refs) (In GER)

## 27. MALIGNANT LYMPHOMAS: CELL SURFACE MARKERS AND ADVANCES IN CLASSIFICATION.

**Strauchen JA**
**VA Medical Center, 3801 Miranda Ave., Palo Alto, CA, 94304**
**West J Med; 135(4):276-284 1981**

Studies of cell surface markers which have led to revise classifications of malignant lymphomas are reviewed. Malignant lymphomas of B cell origin include well-differentiated lymphocytic lymphoma, small lymphocytic lymphoma, low-grade lymphoma, and small lymphocytic lymphoma. These lymphomas and chronic lymphocytic leukemia are morphologically indistinguishable and are almost always B cell neoplasms which demonstrate surface immunoglobulin (SIg) and receptors for complement. Nodular lymphomas are composed of monoclonal B cells which possess a high-density pattern of SIg and a strong complement receptor. Immunologic marker studies suggest that Burkitt's lymphoma cells are rapidly proliferating B cells. In most studies, the large cell lymphomas which are immunologically heterogeneous have been shown to arise most commonly from B cells. The lymphoblastic lymphomas have the features of immature thymic-type T cells. More than half the cases from E rosettes and terminal deoxynucleotidyl transferase is almost always present. Marker studies have demonstrated that Sezary syndrome and mycosis fungoides cells are mature T cells. The nature of the Reed-Sternberg cell which is diagnostic of Hodgkin's disease has not yet been determined.

The application of cell surface marker studies to the classification of lymphomas should greatly enhance the clinical management of these diseases. (56 Refs)

### 28. LYMPHOBLASTIC LYMPHOMA/LEUKEMIA OF T-CELL ORIGIN: ULTRASTRUCTURAL, CYTOCHEMICAL, AND IMMUNOLOGIC FEATURES OF TEN CASES.

Navas Palacios JJ, Valdes MD, Palmes MA, De Salazard MD, Marcilla AG
Departmento de Anatomia Patologica, C.S.S.S. '1 de Octubre,', Carretera de Andalucia Km. 5,4, Madfrid, 26, Spain
Cancer; 48(9):1982-1991 1981

Ten cases of T-lymphoblastic lymphoma/leukemia were studied with light and electron microscopy. Cytochemical stains were performed on touch preparations, and mononuclear cell suspensions were tested for spontaneous rosette formation with sheep RBC, C3 receptors, and surface Ig. The present investigation was performed to evaluate several ultrastructural parameters, mainly the nuclear shape, as diagnostic clues for this group of lymphomas. Characteristic convoluted nuclei were present in 7 to 47% of the lymphoblasts. This percentage correlated with the focal acid phosphatase reaction and E-rosette formation. Acid phosphatase was the best cytochemical marker (7-100% of the lymphoblasts showed focal reaction product). By ultrastructural cytochemistry, the reaction product was demonstrated in the Golgi cisternae and primary lysosomes. The cell suspensions obtained from different sources contained 14 to 95% E-rosette-forming cells. No specific morphologic, cytochemical, or immunologic differences were found between patients with or without mediastinal involvement. (Author abstract) (63 Refs)

### 29. A CRITICAL REVIEW OF THE LITERATURE ON HAIRY CELL LEUKEMIA. SECOND PART: THE ORIGIN OF THE HAIRY CELL.

Bernadou A
Centre de Diagnostic, Hotel-Dieu, 1, place du Parvis Notre-Dame, 75181 Paris, France
Sem Hop Paris; 57(33-36):1380-1385 1981

Studies on the cellular origin of hairy cell leukemia (HCL) are reviewed. Arguments for the monocyte origin of the hairy cell (HC) are questionable. These include morphologic, cytochemical, functional, and immunologic arguments. More recent and convincing studies have investigated the immunological aspects of the HC. The presence of a single type of surface immunoglobulin on the HC is a strong argument in favor of their B lymphocyte origin. Other findings supporting a B cell origin include intracytoplasmic immunoglobulin, secretions of immunoglobulin by the HC, the culture of HC leading to B or T cell markers, rosette formation with mouse red blood cells, and the association of HCL with paraproteinemias. Recent studies have indicated the T cell origin of HCL. Findings include rosette formation of T cell markers on HC, cytotoxicity of anti-T sera to HC, and the persistance of T cell markers on continuous lines of cultured HC. It is suggested that the HC arises from heterogeneous cell lines and that proliferative cells of different origins are responsible for HCL. (134 Refs) (In FRE)

### 30. INTRINSICALLY DEFECTIVE OR EXHAUSTED PLATELETS IN HAIRY CELL LEUKEMIA?

Nenci GG, Gresele P, Agnelli G, Parise P
Inst. Semeiotica Medica, Univ. Perugia Medical Sch., 06100 Perugia, Italy
Thromb Haemost; 46(2):572 1981

Radioimmunoassays of two specific markers of in vivo platelet release reaction (beta-thromboglobulin and platelet factor 4) were performed on the plasma and platelets of three previously untreated patients with hairy cell leukemia (HCL). Results suggest that the storage pool disease-like defect seen in HCL is due to platelets that have undergone the release reaction. Platelets in HCL are not intrinsically defective, but 'exhausted,' thus contradicting one argument in favor of the myeloproliferative origin of HCL. (7 Refs)

### 31. LYMPHOCYTIC LYMPHOMA SIMULATING HAIRY CELL LEUKEMIA: A CONSIDERATION OF RELIABLE AND UNRELIABLE DIAGNOSTIC FEATURES.

Palutke M, Tabaczka P, Mirchandani I, Goldfarb S
Dept. Pathology, Wayne State Univ. Sch. Medicine, 540 East Canfield Ave., Detroit, MI, 48201
Cancer; 48(9):2047-2055 1981

Morphologic, immunologic and functional characteristics of an unusual poorly differentiated diffuse lymphocytic lymphoma closely resembling hairy cell leukemia are presented and the diagnostic features of the latter disease are reviewed. The malignant cells morphologically resembled hairy cells at the light as well as electron microscopic level. They had surface characteristics of both T and B lymphocytes, were phagocytic, and adhered to glass. The spleen was smooth and resembled that seen in hairy cell leukemia. Although there was a predilection for the red pulp of the spleen, there was a lack of characteristic pseudosinus formation, and areas of predominantly white pulp involvement considered characteristic of lymphocytic lymphoma were found after extensive examination. (Author abstract) (26 Refs)

### 32. METHODS AND CLINICAL RELEVANCE OF TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE DETERMINATION IN LEUKEMIC CELLS.

Mertelsmann R, Moore MA, Clarkson B
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Haematol Blood Transfus; 26:68-72 1981

Current technology for the demonstration of terminal deoxynucleotidyl transferase (TdT) is reviewed. The significance of TdT in the clinical and pathophysiologic evaluation of human leukemias and lymphomas is discussed. In acute leukemias, the highest levels of TdT activity are found in approx 95% of non-T, non-B, and T cell acute lymphoblastic leukemias. Elevated levels of TdT have also been observed in some patients with acute nonlymphoblastic leukemia. All myeloproliferative syndromes (MPS: polycythemia vera and chronic myeloid leukemia) and myelodysplastic syndromes (MDS) were found to be TdT- during the chronic phase of their disease; approx 30% of blast phase chronic myeloid leukemias and 15% of other MDS and MPS terminating in acute leukemia were found to exhibit high levels of TdT activity. In patients with lymphoblastic lymphomas of the T and null cell type, high levels of TdT were observed. Lymphoproliferative diseases of the mature T and B cell type have been found to be TdT-. The significance of TdT markers for diagnosis, therapy planning, and prognosis is discussed. The relationship of TdT determinations to moni-

toring of disease activity in TdT+ neoplasia is considered. The determination of TdT activity and definition of cell phenotypes in hematopoietic malignancies may be useful tools for classification of these disorders and may have significant prognostic, clinical, and pathogenetic implications. (17 Refs)

### 33. PROLYMPHOCYTIC LEUKEMIA.

**Ralfkiaer E, Plesner T, Hansen MM, Andersen C, Hou-Jensen K**
**Patologiafdelingen, Finseninstitutet, DK-2100 Copenhagen O, Denmark**
**Ugeskr Laeger; 143(37):2339-2343 1981**

Recent studies on prolymphocytic leukemia (PLL) are reviewed. In a series of 53 patients, there were 32 men and 21 women (40-87 yr old, median age 67 yr). Splenomegaly was found in 53/53 cases, hepatomegaly in 25/53, lymph node involvement in 10/53, skin infiltration in 8/53, lymphocytosis in 53/53, anemia in 50/50, and thrombocytopenia in 31/50. The immunological characteristics were investigated in 34 patients: B-cell markers were found 23/34 cases, T-cell markers in 10/34, and both B- and T-cell markers in 1/34. Dominance of prolymphocytes with typical nuclear structure in the blood and bone marrow is characteristic of PLL. The cases derived from B lymphocytes appear to be related immunologically to non-Hodgkin's lymphoma, and the B prolymphocyte can be differentiated immunologically from the lymphocyte of B-cell chronic lymphocytic leukemia. The survival of the patients is short, ranging from wk to mo, and the patients do not respond to the current therapy for chronic lymphocytic leukemia. The best therapeutic results to date are achieved by splenectomy combined with leukapheresis or polychemotherapy as employed in non-Hodgkin's lymphoma. (28 Refs) (In DAN)

### 34. CELL-BOUND IMMUNOGLOBULIN ON PERIPHERAL BLOOD MONONUCLEAR CELLS OF PATIENTS WITH MYELOMA.

**King MA, Wells JV**
**Kolling Inst. Medical Res., Royal North Shore Hosp. Sydney, St. Leonards, 2065 NSW, Australia**
**Clin Exp Immunol; 45(3):552-556 1981**

Four patients who had myeloma were examined for monoclonal lymphocytes in the peripheral blood using anti-idiotype antibodies. All the patients had received treatment and two were in apparent complete remission. In no case was there any evidence of peripheral blood mononuclear cells (PBMC) with endogenous surface idiotypic determinants, even in patients with active disease. It was found, however, that substantial cytophilic IgG may remain bound to Fc receptors on PBMC even after extensive incubation and washing at 37 C. (Author abstract) (19 Refs)

### 35. ALTERATIONS OF PERIPHERAL BLOOD B-LYMPHOCYTE POPULATIONS IN PLASMA CELL DISORDERS.

**Dillman RO, Royston I, Meserve BL, Griffiths JC**
**Div. Hematology/Oncology V111E, Veterans Admin. Medical Center, San Diego, CA, 92161**
**Cancer; 48(10):2211-2217 1981**

Peripheral blood lymphocytes of patients with multiple myeloma, macroglobulinemia, and monoclonal gammopathy of uncertain significance were analyzed for B cells, and cells bearing kappa light chains and lambda light chains on their surfaces. Compared with controls, the number of B cells were decreased in all three groups. Contrary to other reports, the authors found a B-cell depression of similar magnitude in patients with untreated myeloma and in those with apparently benign monoclonal gammopathy. There was no difference between treated and untreated myeloma patients as a group, or as individuals studied before and after treatment. However, in comparison to control patients, alkylator therapy depressed the WBC count, lymphocyte count, and B-cell number both in the myeloma and in the macroglobulinemia groups. All five patients with previously untreated macroglobulinemia had an increased proportion of circulating lymphocytes with surface light chains of the same type as the M protein. Two patients with IgG myeloma-like disorders had increased circulating B cells with monoclonal surface light chains. This study supports the concepts that normal B cells are depressed in plasma cell disorders, and that abnormal B cells, which are apparently monoclonal, do circulate in some cases. Our results are compared with other published data. (Author abstract) (38 Refs)

### 36. CHEMICAL CHARACTERIZATION OF NEUTRAL GLYCOLIPIDS IN HUMAN MYELOID LEUKEMIAS.

**Klock JC, D'Angona JL, Macher BA**
**Cancer Res. Inst., Dept. Medicine, Univ. California, San Francisco, CA, 94143**
**J Lipid Res; 22(7):1079-1083 1981**

Human neutrophils and lymphocytes have been shown to have different classes of neutral glycolipids. We have investigated alterations of glycolipids in the human myeloid leukemias to see how their neutral glycolipids differ from those of normal neutrophils. The chemical structures of the neutral glycolipids from large numbers of homogeneously purified leukemia cells were determined using column and thin-layer chromatography, gas-liquid chromatography (GLC), GLC-mass spectrometry, and direct probe mass spectrometry. Our results showed that cells from patients with acute myelogenous leukemia (AML) had less than half the amount of neutral glycolipid per cell than did cells from patients with chronic myelogenous leukemia (CML). Chromatographic mapping of the neutral glycolipids from these cells showed that AML cells had less of the polar, long-chain neutral glycolipids than did CML cells. The studies confirmed that over 99% of the neutral glycolipids were contained in a population of compounds with 1, 2, 3, and 4 sugar-containing neutral glycolipids. Lactosyl ceramide was the major glycolipid in both AML and CML cells. The studies show that human myeloid leukemia cells have the same neutral glycolipids as normal neutrophils. The alterations in neutral glycolipid distribution in leukemia suggest that they might be useful as 'differentiation markers', with the morphologically more 'mature' leukemias having more complex glycolipids. We were unable to detect novel or 'malignancy-associated' neutral glycolipids in any of the leukemias we studied. (Author abstract) (15 Refs)

### 37. SOME RECENT TRENDS IN STUDIES OF HUMAN LYMPHOID CELLS: B-CELLS, EPSTEIN-BARR VIRUS, AND TRANSFORMATION.

**Zeuthen J, Klein G**
**Institute for Human Genetics, Bartholin Byggningen, Aarhus Univ., 8090 Aarhus C, Denmark**
**Haematol Blood Transfus; 26:179-190 1981**

A review of recent findings in work on regulatory mechanisms involved in the selective expression of differentiated markers in human B-cell lines and the types of controls involved in the expression and function of Epstein-Barr virus (EBV)-associated markers in human cells, with special attention to the relationship between the expression of EBV func-

tions and the expression of transformation. Because EBV is a lymphotropic virus in man, infection of lymphoid cell lines is reviewed. Chromosome studies on lymphoblastoid cell lines and B-cell lines of BL origin with regard to ploidy and karyotype abnormalities following EBV infection are discussed in detail. Studies of the immunoglobulins synthesized and the major histocompatibility antigens expressed by hybrid lymphocytes are presented. The expression of EBV, the EBV-determined nuclear antigen, and cell transformation by EBV are thoroughly reviewed. (79 Refs)

### 38. SECOND ANNUAL REPORT ON NATIONAL CANCER INSTITUTE AND ENVIRONMENTAL PROTECTION AGENCY PROJECTS.

Department of Health and Human Services
Public Health Service, NIH, Bethesda, MD
Second Annual Report on National Cancer Institute and Environmental Protection Agency Projects. Bethesda, MD, National Cancer Institute, 384 pp., 1981.

Current projects underway under the auspices of the National Cancer Institute and the Environmental Protection Agency are described. Progress reports are presented for the following: a data base for chemicals identified in human biological media, in vivo analysis of UV-B-induced photooxidations; use of the hairless mice for carcinogenesis studies; chronic toxicity and carcinogenicity to rats and mice of chloroform in drinking water; the effects of carcinogens, mutagens, and teratogens on non-human (aquatic) species; the cost effectiveness of two types of personal UV-B dosimeters; the effects of varying doses of UV on mammalian skin; immunodiagnostic markers for breast cancer; antigens on human lymphoid organs for the immunodiagnosis of leukemias and lymphomas; human epithelial cell metabolic activation systems for use with human cell mutagenesis; evaluation of the transformation assay using C3H 10T1/2 cells for use in screening chemicals for carcinogenic potential; national mortality data bases for environmental epidemiology; epidemiologic field studies on ecological relationships between specified toxic substances and cancer morbidity and mortality; an epidemiologic study of populations in Turkey previously exposed to hexachlorobenzene; a case control study of lung, pancreas, and stomach cancer in Southern Louisiana; support services for epidemiologic studies of lung cancer in communities with non-ferrous smelters; an epidemiologic study of the incidence of cancer as related to industrial emissions in the heavily industrialized parts of Contra Costa County in California, an environmental data base for New Jersey to be used in epidemiological studies; an etiologic study of respiratory cancer in coastal Texas; and completion of the NCI/NCHS cooperative study of 1972 mortality data. (no Refs)

## DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS

### 39. USE OF CELL DIFFERENTIATION EFFECTS TO SELECT A HUMAN B LYMPHOBLASTOID CELL LINE ENRICHED IN C3B RECEPTORS.

Barel M, Charriaut C, Frade R
(c/o Frade), Hopital Paul Brouse, I.C.I.G. INSERM U 50 and Association Claude Bernard, 94800 Villejuif, France
J Immunol Methods; 46(2):187-195 1981

A study was undertaken to establish conditions of growth to increase C3b receptor synthesis on a human B lymphoblastoid cell line (Raji) by use of cell differentiation effectors. It appears that whereas two polar compounds HMBA (2 mM) and Me2SO (2%) have no or little effect, 5 BrdU (30 uM) and db cAMP (5 x 10(-4) M) are able to increase in 48 hr and 36 hr respectively the synthesis of C3b receptor on Raji cell surface. These two compounds help to select a variant in which 100% of cells have C3b receptors with a high density of receptors per cell. The mechanism of BrdU action on the regulation of C3b receptor synthesis is discussed. (Author abstract) (23 Refs)

### 40. DETECTION OF CELL-SURFACE ANTIGENS IN MURINE TUMORS BY A PROTEIN A IMMUNOFLUORESCENCE TEST.

Luis J, Merino F
Dept. Experimental Medicine, Instituto Venezolano de Investigaciones Cientificas, Aptdo. 1827, Caracas, Venezuela
Int Arch Allergy Appl Immunol; 66(2):121-130 1981

The detection of antibodies to H-2 and species cell-surface antigens, on suspensions of leukemia and MC-induced sarcomas by an assay using fluorescein-labelled protein A from Staphylococcus aureus is described. The presence of 'foreign' H-2 allospecificities on MC-induced sarcoma cells were detected. Antibodies to leukemia and MC sarcoma cells showed a high degree of cross-reactivity in their reaction with different MC-induced sarcomas and with leukemia cells. (Author abstract) (23 Refs)

### 41. SYNTHESIS AND PROCESSING OF THE ALPHA HEAVY CHAINS OF SECRETED AND MEMBRANE-BOUND IGA.

Kikutani H, Sitia R, Good RA, Stavnezer J
Third Dept. Internal Medicine, Osaka Univ. Medical Sch., Fukushima-ku Osaka 553, Japan
Proc Natl Acad Sci USA; 78(10):6436-6440 1981

We have compared the synthesis and processing of Ig alpha chains in two murine cell lines, a B cell lymphoma that expresses membrane-bound IgA and a hybridoma that secretes IgA. Results of biosynthetic labeling experiments demonstrated that membrane-bound and secreted alpha chains have two distinct intracellular precursors, of different mol wt and isoelectric points. RNAs from both of these cell lines direct the synthesis in vitro of two alpha polypeptides of Mr 59,000 and 62,000, the larger one being the precursor for membrane-bound alpha chain and the smaller one being the precursor for secreted alpha chain. These cell lines each contain three RNAs, 1.7, 2.1, and 3.1 kilobases in length, which hybridize with cDNA for the alpha constant region and which are present in different concentrations. Our results suggest that the smallest RNA encodes the secreted alpha chain and one or both of the larger RNAs encode(s) the membrane-bound alpha chain. (Author abstract) (33 Refs)

### 42. THE USE OF BACTERIA AS MARKERS OF LEUKEMIC LYMPHOCYTES AND FOR THE ISOLATION OF NATURAL KILLER CELLS.

Teodorescu M, Hsu C, Bratescu A, DeBoer KP, Nelson R, Kleinman R, Wen CM, Mayer EP, Pang EJ
Dept. Microbiology, Medical Center, Univ. Illinois, Chicago, IL, 60612
Haematol Blood Transfus; 26:355-359 1981

A method was developed to separate various lymphocyte populations by bacterial adherence and functional difference. The mechanism of natural binding of bacteria to lymphocytes

involves a lectin on the lymphocyte surface and a carbohydrate on the bacterium. Natural killer (NK) cells can be separated by negative selection using monolayers of bacteria. A subpopulation of T cells identified by binding to B globigii was shown to be suppressor for NK cells. Lymphocytes of 5/12 patients with acute lymphocytic leukemia were classified as pre-B cells based on a relatively low percentage of immunoglobulin positive (Ig+) cells but high percentage of lymphocytes binding Brucella melitensis (Bm), a B cell marker independent of surface Ig. Although the percentage of Ig-Bm+ cells was high in all five patients, the percentage of Ig+ cells was relatively low with a relatively normal chi/lambda ratio, suggesting that the cells were arrested at a stage of differentiation much earlier than that in which the surface Ig is exposed. Existence in one patient of a higher percentage of Ig+ cells than cells binding B melitensis suggests that the Ig may sometimes be exogenous. A patient with familial chronic myelocytic leukemia exhibited a relatively high percentage of B m+ lymphocytes which was greater in peripheral blood than in bone marrow. Percentage of Ig+ cells was normal. This observation suggests that B cells and myelocytes may have an immediate common precursor. (13 Refs)

### 43. EXPRESSION OF CHRONIC MYELOID LEUKAEMIA-ASSOCIATED CHANGES IN MEMBRANE GLYCOPEPTIDES IN SOMATIC CELL HYBRIDS.

**Geurts van Kessel AH, Smets LA, Van Rooy H, Hagemeijer A**
**Dept. Cell Biology and Genetics, Erasmus Univ., Rotterdam, The Netherlands**
**J Cell Sci; 51:121-130 1981**

Hybrid cell lines, derived from fusion of rodent cells with peripheral WBC from patients with chronic myeloid leukemia (CML) and from normal donors, were assayed for the presence of CML-associated changes in the carbohydrate moieties of membrane glycoproteins. Expression of this characteristic phenotype did occur in several hybrid clones derived from fusions both with leukemic and normal human WBC. But, expression was only observed when tumorigenic rodent cells were used as fusion partners, and was not observed after fusion with non-tumorigenic rodent cells. Chromosome analysis of the hybrid cells did not reveal a single human chromosome- or chromosomal aberration (eg the Philadelphia chromosome)-bearing factor(s) responsible for this expression. The phenotypic expression observed could be due to dissociation of certain human genes from their regulator(s), as a result of chromosome loss in interspecific cell hybrids. (Author abstract) (19 Refs)

### 44. FC AND C3B RECEPTORS ON CULTURED RETINOBLASTOMA CELLS.

**Stein PC, Rand N, Char DH**
**Ocular Oncology Unit, Univ. California Medical Center, San Francisco, CA, 94143**
**Invest Ophthalmol Vis Sci; 21(4):550-553 1981**

Fc and C36 receptors were investigated to determine their presence on retinoblastoma tissue culture cells. Various techniques including radioiodination, polyacrylamide gel electrophoresis (PAGE) immunoprecipitation, affinity chromatography, and rosette assays were used to investigate tumor cells, normal human retinal pigment epithelium (RPE), and three lymphoblastoid cell lines. Results show that detergent extracts from surface labeled retinoblastoma cells bound to affinity gels prepared with human IgG, aggregated IgG, and Fc but not to control gels prepared from Fab'2 or Sepharose-4B alone. Elected cell lysate proteins were partially characterized by PAGE and autoradiography. Protein bands had mol wt of approx 4.3 x 10(4) daltons. Cultured retinoblastoma cells were found to rosette with human indicator RBC specific for C3b and Fc receptors. These results suggest that binding of serum components from retinoblastoma patients to cultured tumor cells may be mediated by Fc and C3b receptors in addition to specific binding to tumor-associated antigens. Future investigations should take steps to eliminate Fc and C3b mediated binding. (11 Refs)

## LYMPHOCYTE AND DIFFERENTIATION ANTIGENS

### 45. DISTRIBUTION OF COMMON ACUTE LYMPHOBLASTIC LEUKEMIA ANTIGEN IN NONHEMATOPOIETIC TISSUES.

**Metzgar RS, Borowitz MJ, Jones NH, Dowell BL**
**Dept. Microbiology, Duke Univ. Medical Center, Durham, NC, 27710**
**J Exp Med; 154(4):1249-1254 1981**

The presence of common acute lymphoblastic leukemia antigen (CALLA) in certain cell types of nonhematopoietic adult and fetal tissues was examined by immunoperoxidase staining with the J-5 monoclonal antibody. Portions of normal tissues were removed during the course of surgery from patients with leukemia or lymphoma and a 20-wk-old fetus was obtained from a prostaglandin-induced abortion. Compared to control ascites fluid from BALB/c mice injected ip with the P3 x 63Ag8 myeloma cell line (P3), no significant staining was found in the fetal heart, liver, lung, pancreas, salivary gland, spleen, or thymus, or in the adult skeletal muscle, spleen, tonsil, salivary gland, small intestine, or colon. However, significant staining was observed in adult kidney, fetal kidney, fetal small intestine, and the myoepithelial cell layer of adult breast. In particular, the J-5 antigen was present on proximal tubules and glomeruli of the kidney. The glomerular staining may have been on the podocyte and not the basement membrane. CALLA was shown to migrate as a 90,000 mol wt antigen rather than the 98,000-100,000 mol wt antigen noted on CALLA-positive tissue culture cell lines. The determinant defined by the J-5 monoclonal antibody may be neither lymphoid cell-specific differentiation antigen nor leukemia-specific antigen. (20 Refs)

### 46. LY 11.2: A CELL SURFACE ANTIGEN THAT MAY IDENTIFY MURINE LYMPHOCYTES SUSCEPTIBLE TO TRANSFORMATION BY ONCOGENIC AGENTS.

**Meruelo D, Paolino A, Flieger N, Offer M, Dworkin J**
**Irvington House Inst., Dept. Pathology, New York Univ. Medical Center, New York, NY, 10016**
**Fed Proc; 40(12):2717-2720 1981**

Ly 11.2, a newly defined T cell surface antigen, is present on two lymphocyte subpopulations playing a key role during leukemogenesis: the natural killer cell and possibly the target cells for malignant transformation by oncogenic agents. Antibodies to this cell surface marker should greatly help in the study, isolation, and characterization of these cells. (Author abstract) (20 Refs)

## 47. AN AUTOANTIBODY REACTIVE WITH NUCLEI OF POLYMORPHONUCLEAR NEUTROPHILS: A CELL DIFFERENTIATION MARKER.

**Whittingham S, Morstyn G, Wilson JW, Vadas MA**
**Clinical Res. Unit., Walter and Eliza Hall Inst. of Medical Res., Royal Melbourne Hosp., Victoria 3050, Australia**
**Blood; 58(4):768-771 1981**

An autoantibody that reacted with nuclei of polymorphonuclear neutrophils (PMN) was detected at titers of greater than 10 in sera of 25 of 50 patients with rheumatoid arthritis and 36 of 50 with autoimmune chronic active hepatitis but in none of 160 controls comprising 24 patients with alcoholic cirrhosis, 36 with multiple myeloma, and 100 healthy subjects. Through the use of enriched populations of hemopoietic cells, this antibody was shown to be cell-specific, reacting only with the nucleus of the mature neutrophil. It was unreactive with nuclei of progenitor cells in the myeloid series and with nuclei of eosinophils, monocytes, lymphocytes, and thymocytes. It reacted with a determinant that appeared to be a differentiation antigen. This cell-specific autoantibody may prove to be of value in analytical studies of granulocyte maturation. (Author abstract) (20 Refs)

## 48. BETA2-MICROGLOBULIN IN CANCER.

**Pesce AJ, Weiss MA, DiPersio L, Michael JG**
**Univ. Cincinati Medical Center, Cincinati, OH**
**IMJ; 160(3):191-195 1981**

Early discovery of the role of beta2-microglobulin (B2m) in cancer is reviewed along with results of various studies. Human B2m was readily identified and quantified in the plasma of athymic mice bearing various human tumors, and the amount in the plasma was directly related to the amount of B2m in tumor extracts. The level of B2m varied widely and was lowest in tumors with the fastest growth rate. Immunofluorescence studies in individual tumor cells showed wide variations in B2m content; some poorly differentiated carcinomas exhibited no B2m. Studies of mouse teratocarcinoma cell lines support the concept that B2m may be a marker of differentiation in cells. Since B2m forms parts of the human histocompatibility antigens, it may serve as a marker for these antigens. Data indicate serum level of B2m can be used to mark cancer if the tumor cells produce large amounts as in lymphoproliferative disorders. A potentially more important use of this marker is in immunohistology, where it might be used to characterize tumor differentiation, heterogeneity, and metastatic capacity.

## 49. EXPRESSION OF MYELOID DIFFERENTIATION ANTIGENS ON NORMAL AND MALIGNANT MYELOID CELLS.

**Griffin JD, Ritz J, Nadler LM, Schlossman SF**
**Div. Tumor Immunology, Sidney Farber Cancer Inst., Harvard Medical Sch., Boston, MA, 02115**
**J Clin Invest; 68(4):932-941 1981**

A series of monoclonal antibodies have been characterized that define four surface antigens (MY3, MY4, MY7, and MY8) of human myeloid cells. They were derived from a fusion of the NS-1 plasmacytoma cell line with splenocytes from a mouse immunized with human acute myelomonocytic leukemia cells. MY3 and MY4 are expressed by normal monocytes and by greater than 90% of patients with acute monocytic leukemia or acute myelomonocytic leukemia, but are detected much less often on other types of myeloid leukemia. MY7 is expressed by granulocytes, monocytes, and 5% of normal bone marrow cells. Seventy nine percen t of all acute myeloblastic leukemia (AML) patients tested (72 patients) express MY7 without preferential expression by any AML subtype. MY8 is expressed by normal monocytes, granulocytes, all peroxidase-positive bone marrow cells, and 50% of AML patients. MY3, MY4, and MY8 define myeloid differentiation antigens in that they are not detected on myeloid precursor cells and appear at discrete stages of differentiation. These antigens are not expressed by lymphocytes, RBC, platelets, or lymphoid malignancies. The monoclonal antisera defining these antigens have been used to study differentiation of normal myeloid cells and malignant myeloid cell lines. (Author abstract) (49 Refs)

## 50. BIOCHEMICAL CHARACTERIZATION OF AN ANTIGEN ASSOCIATED WITH ACUTE LYMPHOBLASTIC LEUKEMIA AND LYMPHOCYTE PRECURSORS.

**Newman RA, Sutherland DR, Greaves MF**
**Imperial Cancer Res. Fund Lab., P.O. Box 123, Lincoln's Inn Field, London WC2A 3 PX, England**
**Haematol Blood Transfus; 26:326-328 1981**

An antigen (ALLA) occurring on the surface membrane of cells from patients with common acute lymphoblastic leukemia (ALL) was previously identified. ALLA was also found in some cases of undifferentiated leukemias and chronic myeloid leukemia and in a small proportion of normal bone marrow cells. ALLA from the cell line Nalm-1 was characterized biochemically. ALLA is a glycosylated polypeptide of approx 100,000 daltons. No intrachain disulfide linkages are present. ALLA shows 50% binding with lentil lectin, but 100% binding with Ricinis communis lectin. Lectin binding and nonbinding forms form identical homogeneous spots in two-dimensional isoelectric focusing with a pI of 5.1-5.5. Neuraminidase treatment of both forms causes a shift of approx 0.6 towards the basic end of the gel. Treatment with tunicamycin and glycosidases indicate that up to 25% of ALLA mol wt may be carbohydrate, but carbohydrate is not involved in the antigenic site. ALLA is apparently not integral to the cell membrane, but is closely associated with it. Presence of ALLA in some normal bone marrow cells suggests the antigen is a normal product reflecting target cells for malignant transformation and/or the stage of maturation arrest of ALL cells. (11 Refs)

## 51. HUMAN LEUCOCYTE ANTIGENS.

**Beverley PC, Linch D, Callard RE**
**ICRF Human Tumour Immunology Group, Univ. London, University St., London WC1E 6JJ, England**
**Haematol Blood Transfus; 26:309-313 1981**

Bone marrow progenitor cells were characterized and stages of T lymphocyte differentiation traced using monoclonal antisera. Bone marrow cells were treated with antimyeloid antibody, which lysed about 50% of the cells, primarily myelocytes and metamyelocytes. After staining with anti-HLe-1 the remaining cells were sorted. Weakly staining cells accounting for less than 2% of total marrow nuclea ted cells were collected. This fraction contained myeloid and erythroid progenitors and cells with the nuclear enzyme TdT. The TdT-bearing cells were probably lymphoid progenitors and had the phenotype HLe+-TG-1-. About 5% of intrathymic cells were large and lacked the cortical thymic marker HTA-1. The earliest cortical cells lacked HLA-A, -B, and -C antigens, which the presumed marrow progenitor cells possessed. Some early cortical cells possessed TdT and OKT9 markers. Medullary cells resembled peripheral T cells in lacking HTA-1 and TdT but regaining

HLA. Thymic phenotypes showed heterogeneity paralleling that shown by leukemic cells, indicating that caution should be used in identifying phenotypes as abnormal. Analysis of peripheral lymphoid cells suggested that UCHT1 antigen is a marker for mature T cells. (17 Refs)

### 52. CYTOTOXIC T CELL RECOGNITION OF EPSTEIN-BARR VIRUS-INFECTED B CELLS. I. SPECIFICITY AND HLA RESTRICTION OF EFFECTOR CELLS REACTIVATED IN VITRO.

Moss DJ, Wallace LE, Rickinson AB, Epstein MA
(c/o Rickinson) Dept. Pathology, Univ. Bristol Medical Sch., University Walk, Bristol BS8 1TD, England
Eur J Immunol; 11(9):686-693 1981

The experiments show that the phenomenon of regression, seen exclusively in Epstein-Barr (EB) virus-infected cultures of mononuclear cells from EB virus antibody-positive donors, is mediated by cytotoxic T cells reactivated in vitro and specifically recognizing an EB virus-induced lymphocyte-detected membrane antigen LYDMA. Thus, effector T cells from regressing cultures kill autologous EB virus-transformed cells but not autologous pokeweed mitogen-stimulated lymphoblasts nor any of a range of EB virus genome-negative human hemopoietic cell lines (K562, HSB2, BJAB, EB4) particularly sensitive to nonspecific natural killer-like activities. Moreover, these reactivated effector cells exhibit classical HLA restriction of target cell recognition; in a survey of 14 effector cell donors, preferential lysis of the autologous virus-transformed line was a consistent feature, while the relative degree of lysis of allogeneic lines was in general directly related to the number of HLA-A and B antigens shared between effector and target cells. The pattern of reactivity shown by effector T cell preparations from any one donor was strikingly reproducible, and the results from a number of donors revealed differences between particular HLA-A and B antigens with respect to the level of EB virus-specific killing which was associated with sharing through these determinants. (Author abstract) (52 Refs)

### 53. CYTOTOXIC T CELL RECOGNITION OF EPSTEIN-BARR VIRUS-INFECTED B CELLS. II. BLOCKING STUDIES WITH MONOCLONAL ANTIBODIES TO HLA DETERMINANTS.

Wallace LE, Moss DJ, Rickinson AB, McMichael AJ, Epstein MA
(c/o Rickinson) Dept. Pathology, Univ. Bristol Medical Sch., University Walk, Br istol BS8 1TD, England
Eur J Immunol; 11(9):694-699 1981

Monoclonal antibodies specifically binding common determinants on all HLA-A, B and C antigen molecules blocked the lysis of EB virus-transformed target cells by EB virus-specific cytotoxic T cells reactivated in vitro. Blocking was mediated through binding of the antibodies to the target rather than to the effector cells and was max (75 to 85% inhibition of lysis) at saturating antibody concentrations. A similar blocking effect was also shown by a monoclonal antibody binding to beta2-microglobulin, a molecule physically associated with HLA-A, B and C antigens on the target cell surface, but not by a monoclonal antibody binding to the non-HLA-associated WBC-common antigen. Saturating concentrations of monoclonal antibodies specific for common determinants on all HLA-DRw antigen molecules either had no effect at all upon EB virus-specific T cell cytotoxicity or caused a slight, but nonspecific, inhibition. The results demonstrate unequivocally that HLA-A, B and C antigens on the target cell surface are indeed the polymorphic elements which impose genetic restriction upon EB virus-specific cytotoxicity T cell function. (Author abstract) (32 Refs)

## CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION

### 54. IMMUNOLOGIC SUBSETS IN HUMAN B-CELL LYMPHOMAS IN RELATION TO NORMAL B-CELL DEVELOPMENT.

Godal T, Lindmo T, Ruud E, Heikkila R, Henriksen A, Steen HB, Marton PF
Norsk Hydro's Inst. for Cancer Res., Montebello, Oslo 3, Norway
Haematol Blood Transfus; 26:314-319 1981

The expression of surface immunoglobulins (Igs), complement receptors, and Ig heavy chains on lymphocytic, centroblastic, centroblastic/centrocytic, and lymphoplasmacytoid lymphomas is reported. All the lymphomas could be triggered to differentiate and synthesize Ig in vitro by anti-Ig in combination with tetradecanoylphorbol acetate. (20 Refs)

### 55. SURFACE CHARACTERISTICS OF THE U-937 HUMAN HISTIOCYTIC LYMPHOMA CELL LINE: SPECIFIC CHANGES DURING INDUCIBLE MORPHOLOGIC AND FUNCTIONAL DIFFERENTIATION IN VITRO.

Nilsson K, Forsbeck K, Gidlund M, Sundstrom C, Totterman T, Sallstrom J, Venge P
The Wallenberg Laboratory, University of Uppsala, Box 562, 75122 Uppsala, Sweden
Haematol Blood Transfus; 26:215-221 1981

The inducible differentiation of the human histiocytic lymphoma cell line U-937 was studied. Morphologic and functional changes can be induced in U-937 cells by the addition of 12-O-tetradecanoyl-phorbol-13-acetate (TPA) or the supernatant of a mixed lymphocyte culture (MLC). TPA treatment caused increased cell clustering, the appearance of a small fraction of adherent cells that increased with time, the acquisition of a macrophage-like morphology, an increase in cell size among cells in free-floatin g clusters, and the expression of several nonspecific esterases. Following TPA or MLC supernatant treatment, U-937 cells expressed different surface glycoproteins that caused them to resemble mature blood monocytes more closely than before treatment. The treated cells became more effective as effector cells in antibody-dependent cellular cytotoxicity tests with antibody-coated chicken erythrocytes, exhibited increased lysozyme secretion, and had the capacity for phagocytosis (which untreated cells did not). It is not yet clear whether all cells or only a fraction of cells respond to the inducive signals from TPA and MLC supernatant or whether 'terminal' differentiation occurs in the U-937 cells. Results do indicate that at least a partial inhibition of growth and DNA synthesis accompany TPA treatment and the described phenotypic alterations. (28 Refs)

### 56. TERMINAL DIFFERENTIATION SURFACE ANTIGENS OF MYELOMONOCYTIC CELLS ARE EXPRESSED IN HUMAN PROMYELOCYTIC LEUKEMIA CELLS (HL60) TREATED WITH CHEMICAL INDUCERS.

Perussia B, Lebman D, Ip S H, Rovera G, Trinchieri G
Wistar Inst. Anatomy and Biology, 36th and Spruce St., Philadelphia, PA, 19104
Blood; 58(4):836-843 1981

The expression of two surface antigens present on the cell membrane of both human granulocytes and monocytes was

studied during the process of myelomonocytic differentiation using two monoclonal antibodies (B9.8.1 and B13.4.1). These surface antigens are not present on immature myeloid cells nor on nonmyeloid hematopoietic cells, but can be detected when the cells are terminally differentiated. Among the bone marrow cells, B13.4.1 binds to metamyelocytes and B9.8.1 to metamyelocytes and a fraction (30%) of myelocytes. HL60 human promyelocytic leukemia cells did not react with such monoclonal antibodies. However, when such cells were induced to differentiate in vitro into mature myeloid elements by treatment with retinoic acid or dimethyl sulfoxide, 70%-90% of the differentiated cells expressed both surface antigens. Cell sorting studies on these treated HL60 cells indicated that myelocytes and metamyelocytes were the most immature cells expressing such markers. Expression of the two surface antigens was also observed when HL60 cells were induced to differentiate into monocyte/macrophage cells by treatment with the tumor promoter 12-0-tetradecanoyl-phorbol-13-acetate. Thus, human promyelocytic leukemia cells induced to differentiate in vitro by treatment with specific chemical agents express membrane antigens in the same pattern as normal bone marrow myeloid cells at the corresponding stage of differentiation. (Author abstract) (26 Refs)

## 57. SURFACE ANALYSIS OF EARLY AND LATE MOPC-315-EL TUMOR CELLS.

**Harris D, Bailey J, Lewis JC, Grover WH, Panetti M, Evans DL, Ruebush MJ, Paulus LK, Burgess D, Hale AH**
**(c/o Hale) Dept. Microbiology, Bowman Gray Sch. Medicine, Winston-Salem, NC, 271 03**
**Cell Immunol; 64(1):119-130 1981**

The surface properties of a tumor line which undergoes a cyclic change in reactivity with cytotoxic T lymphocytes (CTLs) have been analyzed. The findings indicate that MOPC-315-EL when transplanted into the peritoneum of a BALB/c mouse for 4-5 days (early MOPC-315-EL) becomes sensitive to lysis by anti-H-2d CTL. After 9 to 10 days of growth in the peritoneal cavity these tumor cells (late MOPC-315-EL) become unreactive to CTLs. The amount of H-2 antigens on the surface of the cells is the same on the early and late tumor cells. By scanning electron microscopy (SEM) we have shown that the early population is a mixture of two cell types which are characterized by surface villi or surface blebs; the late cells are essentially one population which are characterized by surface villi. The net charge on the surface of the cell was evaluated by two methods: (i) rate of cell migration across an electric potential and (ii) binding by cationic ferritin to the glycocalyx. Both techniques indicated that the early cells have a higher net negative charge. The implication of this work is that surface charge may be involved in T cell-target interactions. (Author abstract) (11 Refs)

## 58. MEMBRANE DIFFERENTIATION IN HUMAN MYELOID CELLS: EXPRESSION OF UNIQUE PROFILES OF CELL SURFACE GLYCOPROTEINS IN MYELOID LEUKEMIC CELL LINES BLOCKED AT DIFFERENT STAGES OF DIFFERENTIATION AND MATURATION.

**Fukuda M, Koeffler HP, Minowada J**
**Biochemical Oncology, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104**
**Proc Natl Acad Sci USA; 78(10):6299-6303 1981**

Cell surface glycoprotein structures of human leukemic cell lines blocked at various stages of myeloid (granulocyte-monocyte) differentiation and maturation were characterized. Cell lines representing early stages of differentiation and maturation such as KG1a, KG1 and those representing later stages such as ML-1-3 and HL-60 were found to express discretely different sets of cell surface glycoproteins. The proteins (such as Gp130) present on mature granulocytes appear only in cell lines representing later stages of maturation. The quantity and structure of the carbohydrate chains susceptible to endo-beta-galactosidase ('lactosaminoglycan') are also significantly different among cell lines. A small quantity of essentially unbranched lactosaminoglycan is present on KG1a and KG1 cells, whereas a significant quantity of branched lactosaminoglycan is present on the more mature ML-1-3 and HL-60 cells. The process of myeloid maturation from promyeloblast to granulocyte is accompanied by the disappearance of the and 95-kilodalton glycoproteins, the appearance of Gp130, and a, great increase in the quantity and branching structure of lactosaminoglycan. These results are discussed together with our previous findings on erythroid dif ferentiation and maturation. (Author abstract) (36 Refs)

## 59. EXPRESSION OF COMMON ACUTE LYMPHOBLASTIC LEUKAEMIA ANTIGEN AND TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE IN NORMAL MONONUCLEAR BLOOD CELLS DURING DIFFUSION CHAMBER CULTURE.

**Jager G, Lau B**
**Institut fur Hamatologie, Landwehrstr. 61, D-8000 Munchen 2, W. Germany**
**Scand J Haematol; 27(1):5-8 1981**

Peripheral mononuclear blood cells of two healthy individuals were cultured over a 13 day period in diffusion chambers. A high percentage of cALL antigen positive cells and later on TdT containing cells appeared during culture. The cALL+ cells could be clearly distinguished into two groups: a population with weak and diffuse fluorescence and a small number of ring-like brightly dyed cells. The first group develops into TdT+ cells and therefore resembles immature T-cells. The interpretation of the ring-like stained cells is still preliminary, but it cannot be excluded, that these cells represent a cell population with more than lymphatic differentiation capacity. (Author abstract) (12 Refs)

## 60. DERIVATION OF HUMAN T-CELL LEUKEMIAS.

**Reinherz EL, Schlossman SF**
**Div. Tumor Immunology, Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115**
**Cancer Res; 41(11,part2):4767-4770 1981**

Cell surface antigenic changes occur during the stages of T-cell ontogeny in several animal model systems. In the present study, multiple monoclonal antibodies were developed to human thymocyte and T-cell surface differentiation antigens as a means of probing T-cell ontogeny in humans. It was shown that three distinct stages of human intrathymic differentiation exist and that the mature inducer (T4+) and suppressor (T5+/TH2+) T-cell subsets arise at specific points during these maturation events. Moreover, T-cell leukemias can now be related to the three stages of the thymic compartment or, alternatively, the more differentiated peripheral T-cell compartment. (Author abstract) (28 Refs)

## EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS

### 61. CELL CYCLE-RELATED MORPHOLOGICAL CHANGES OF FELINE LYMPHOID CELLS AS REVEALED BY ELECTRON MICROSCOPY.

**Toth SR**

**Dept. Veterinary Pathology, Univ. Glasgow Veterinary Sch., Bearsden Road, Bearsden, Glasgow, G61 1QH, Scotland**

**Cancer Res; 41(11,part1):4727-4736 1981**

The aim of this study was to correlate morphological changes in cells to known phases of the cell cycle. For this purpose, feline lymphoblastoid cells (FL74) chronically infected with feline leukemia virus were synchronized and examined by scanning and transmission electron microscopy. Scanning electron microscopy revealed that the cell surface underwent distinct changes which were found to be cell cycle specific. Morphological changes shown by transmission electron microscopy were used as ult rastructural markers to confirm the findings made by scanning electron microscopy relating to the various phases of the cell cycle. The results of these experiments suggest that the presence of morphologically mixed populations of cells in many lymphoproliferative disorders, which had been described previously, may be explained by normal cell cycle-dependent variations. (Author abstract) (32 Refs)

### 62. 1ALPHA,25-DIHYDROXYVITAMIN D3 INDUCES DIFFERENTIATION OF HUMAN MYELOID LEUKEMIA CELLS.

**Miyaura C, Abe E, Kuribayashi T, Tanaka H, Konno K, Nishii Y, Suda T**

**(c/o Suda) Dept. Biochemistry, Sch. Dentistry, Showa Univ., 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142, Japan**

**Biochem Biophys Res Commun; 102(3):937-943 1981**

Human promyelocytic leukemia (HL-60) cells were inoculated at 1 x 10(5) cells/ml on day 0 and incubated for 4 days. Cell suspensions were grown without (control) or with 1.2 x 10(-10), 1.2 x 10(-9), or 1.2 x 10(-8) M 1alpha,25-dihydroxyvitamin D3 (D3). Cell growth was inhibited in a dose- and time-dependent manner; inhibition was effected at 10(-9) M D3 and at 10(-8) M D3 viable cell count was decreased to 20% of control. Addition of 1.2 x 10(-8) M D3 induced 41% of cells to differentiate from promyelocytes with large round nuclei into myeloid cells including myelocytes and metamyelocytes; 3% differentiated into mature granulocytes. Inducing activity of D3 was similar to that found with dimethyl sulfoxide (DMSO) and actinomycin D but not 12-O-tetradecanoyl-phorbol-13-acetate (TPA). Incubation of HL-60 with D3 induced cell adhesion to dish surfaces, phagocytic activity, and rosette formation. With 1.2 x 10(-8) M D3, 53% of cells became phagocytic vs 6.3% of controls; C3 receptor formation was seen in 57% vs 9.5% of control cells. Formation of Fc receptors was not affected by D3. Similar results were obtained with DMSO, actinomycin D, and TPA, except that TPA slightly induced formation of Fc receptors. Results indicate that, like TPA, DMSO, and actinomycin D, D3 at physiological plasma concentrations is involved in cell growth and differentiation of human myeloid leukemia cells. (19 Refs)

### 63. MATURATION OF HUMAN PERIPHERAL BLOOD LEUKEMIC CELLS IN SHORT-TERM CULTURE.

**Forbes P, Dobbie D, Powles R, Alexander P**

**Chester Beatty Res. Inst., Clifton Ave., Belmont, Sutton, Surrey SM2 5PX, England**

**Haematol Blood Transfus; 26:268-271 1981**

The effects of dimethylsulfoxide (DMSO), thioproline and prostaglandins A1 and A2 were studied in acute myelogenous leukemia (AML) cells. Exposure to DMSO did not affect the patterns of maturation observed. Increased concentrations of prostaglandins resulted in an increase of the percentage of chloracetate esterase positive cells seen. The prostaglandins also raised the percentage of Fc receptor positive cells but did not affect the numbers of adherent and nonadherent cells. No significant effect was seen in the cultures containing thioproline. (6 Refs)

### 64. TUMOR-PROMOTING PHORBOL DIESTER-INDUCED SPECIFIC CHANGES IN CELL SURFACE GLYCOPROTEIN PROFILE OF K562 HUMAN LEUKEMIC CELLS.

**Fukuda M**

**Biochemical Oncology, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104**

**Cancer Res; 41(11,part1):4621-4628 1981**

The tumor-promoting phorbol ester, 12-O-tetradecanoylphorbol-13-acetate (TPA), induced specific changes in the cell surface glycoprotein profile of K562 human leukemic cells. TPA-treated K562 cells were examined by cell surface labeling followed by immunoprecipitation with anti-glycophorin antiserum or anti-K562 antiserum. TPA-treated K562 cells lost glycophorin and glycoprotein with a mol wt of 105,000, which are specific to later stages of erythroid cell differentiation, and retained glycoprotein with a mol wt of 95,000, which is specific to early stages of erythroid cell differentiation. On the other hand, 4alpha-phorbol-12,13-didecanoate, which is inactive as a tumor promoter, induced no significant changes in cell surface glycoproteins of K562 cells. In parallel, TPA induced morphological changes of K562 cells as their growth was inhibited, whereas 4alpha-phorbol-12,13-didecanoate had no effect on these two characteristics. Thus, the tumor promoter induced specific changes in the cell surface glycoprotein profile of K562 human leukemic cells, which appeared to be induced into a retrodifferentiated stage. (Author abstract) (51 Refs)

### 65. TPA-INDUCED SURFACE MEMBRANE CHANGES IN HUMAN LEUKEMIA/LYMPHOMA CELLS (MEETING ABSTRACT).

**Nilsson K, Totterman TH**

**The Wallenberg Laboratory and Department of Internal Medicine, Uppsala University, Box 562, S-751 22 Uppsala, Sweden**

**Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland. The Congress 92 pp., 1981.**

Phorbol ester (tetradecanoylphorbol acetate, TPA)-induced, differentiation-associated phenotypic and functional cellular changes were studied in two separate systems, ie the human histiocytic lymphoma cell line U-937 and biopsy cells from patients with chronic lymphocytic leukemic (CLL). In U-937, low concentrations of TPA (or MLC supernatant) effected the morphological maturation from monoblasts to adherent macrophages, together with an increase in the expression of non-specific esterases, phagocytosis, lysozyme secretion, surface IgG-Fc receptors and Ia molecules. Differentiated U-937 cells

became active as effectors in antibody dependent cellular cytotoxicity, and their sensitivity to lysis by natural killer (NK) cells decreased. TPA-driven differentiation of U-937 cells was associated with changes in cell surface glycoprotein (GP) and glycolipid (GL) patterns towards mature monocytes. In CLL cultures, TPA-induced, a lymphoblast morphology with cluster formation, synthesis of cytoplasmic heavy and light Ig chains and I a-like antigens, and an increased secretion of interferon and beta2-microglobulin. Cell surface changes induced in CLL cells by TPA were evidenced by a decreased expression of Fc and mouse RBC receptors and Ia-like antigens, by an increased susceptibility to both allogeneic and autologous NK cells and by changes in the GL patterns. In conclusion, TPA is capable of inducing phenotypic and functional changes in leukemia/lymphoma cells which presents an opportunity to detailed in vitro studies on the differentiation process. The observed alterations in GP/GL patterns can prove helpful in the characterization of cell surface target structures for the NK cell lytic attack. (no Refs)

## 66. TUMOR PROMOTER PHORBOL MYRISTIC ACETATE STIMULATES IMMUNOGLOBULIN SECRETION CORRELATED WITH GROWTH CESSATION IN HUMAN B LYMPHOCYTE CELL LINES.

**Ralph P, Kishimoto T**
**Dept. Developmental Hematopoiesis, Memorial Sloan-Kettering Cancer Center, Rye, NY, 10580**
**J Clin Invest; 68(4):1093-1096 1981**

Ig production by lymphoblast cell lines was studied using protein A-RBC plaque formation to detect individual secreting cells. Ig secretion by 6 of 12 human B-cell lines tested could be stimulated up to 20-fold by phorbol myristic acetate (PMA) at subtoxic concentrations of 10-1,000 ng/ml depending on the line. Stimulation was found with both IgM and IgG cell lines. No switch of Ig class synthesis was found in the cell lines as a result of PMA incubation. Increase in Ig secretion was closely associated with cessation of growth resembling induction of terminal differentiation in the cells. PMA induction of Ig secretion in B lymphocytes from normal peripheral blood requires the cooperation of T cells. PMA stimulation of certain cell lines reported here suggests that the lines are late in the differentiation pathway to plasmacyte and can be easily triggered to secrete Ig by membrane-altering agents. (Author abstract) (27 Refs)

## 67. MANIFESTATIONS OF CELLULAR IMMUNITY IN THE RAT AFTER PROLONGED ASBESTOS INHALATION. II. ALVEOLAR MACROPHAGE-INDUCED SPLENIC LYMPHOCYTE PROLIFERATION.

**Miller K, Kagan E**
**(c/o Kagan) Dept. Pathology, Georgetown Univ. Sch. Medicine, 3900 Reservoir Road, N.W., Washington, DC, 20007**
**Environ Res; 26(1):182-194 1981**

The present study has shown that alveolar macrophages from asbestos-exposed rats (dusted macrophages) can induce the proliferation of autologous splenic lymphocytes (dusted lymphocytes) as well as the proliferation of syngeneic lymphocytes from control nonexposed rats (control lymphocytes). Significant lymphoproliferation did not occur when alveolar macrophages from control rats (control macrophages) were cocultured with control or dusted splenic lymphocytes for similar periods of time (72 or 96 hr). The activation of control lymphocytes by dusted macrophages was similar, in some respects, to the lymphopr oliferative response evoked by sodium periodate-treated control macrophages, since both these reactions peaked at 72 hr and were abolished by treatment of the macrophages with the reducing agent, L-cysteine. This periodate-like response produced by dusted macrophages appears to result from aldehyde-like modifications on the macrophage cell membrane. L-Cysteine treatment did not, however, affect the blastogenic response induced by dusted macrophages on dusted lymphocytes, which peaked at 96 hr. Since the in vitro addition of crocidolite to cell cultures did not trigger lymphoproliferation, these collective findings suggest the expression of asbestos-related antigen-like determinants on the surface of dusted macrophages. We conclude that the proliferative reactions induced in splenic lymphocytes by dusted macrophages were a consequence of two different phenomena:a periodate-like effect (noted in control lymphocytes) and an effect produced by a putative asbestos-related, macrophage-associated antigen (observed in dusted lymphocytes). (Author abstract) (43 Refs)

## 68. EFFECT OF RADIATION AND CHEMOTHERAPY AND REACTIVITY OF LYMPHOCYTE SUBPOPULATIONS (MEETING ABSTRACT).

**Gerber M, Serrou B**
**Labortoire d'Immunopharmacologie des Tumeurs, FRA-INSERM 46, 34033 Montpellier Cedex, France**
**Long Term Normal Tissue Effects of Cancer Treatment, April 13-15, 1981, Bethesda, Maryland Committee for Radiation Oncology Studies; 1981**

In allogeneic system, sensitization of the cytotoxic T lymphocytes (CTL) has been shown to be sensitive to both low doses of cyclophosphamide (Cy) and low doses of irradiation. Cy (48 mg/kg) inhibited the activity of mouse CTL when administered at the time of immunization but it was associated with a normal graft rejection, suggesting that other mechanisms resistant to Cy were involved in graft rejection. Methyl-Prednisolone (5 mg/kg) had little effect on cytotoxicity but was nevertheless associated with graft facilitation. On the contrary low dose irradiation (0.15 Gy) administered 2 to 4 days after allogeneic tumor cells transplantation not only decreased in vitro CTL activity but also inhibited the graft rejection. Moreover, in a syngeneic tumoral system, it was shown that the scattering dose of 7 Gy (0.12 to 0.15 Gy at the spleen) administered as localized radiotherapy was significantly decreasing the T-cell cytotoxic activity against the relevant tumoral antigen. In addition, it was shown that the better results of a second radiotherapeutic regimen (a dose of 4 Gy with a scatter dose inferior to 0.15 Gy) were abolished by a previous immunosuppression, suggesting the participation of the T-cell response in the final outcome of localized radiotherapy. In vitro allogeneic studies were undertaken to further investigate the radiosensitive step of this cytotoxic response. The irradiation had to be delivered at the time of mouse splenocyte sensitizatio n in mixed lymphocyte culture in order to decrease significantly the cytotoxic response generated in the mixed culture. Nylon wool column depletion and use of anti-Thy 1-2 serum plus complement demonstrated that the radiosensitive cytotoxic cells were non adherent T cells. Decreased cytotoxicity is still shown after early and late restimulation. The later observation and the requirement for irradiation at the time of sensitization strongly suggest that antigen recognition and the akin phenomenons (maturation of cytotoxic lymphocyte precursor, acquisition of a receptor), might be the radiosensitive step. (no Refs)

### 69. IN VITRO EFFECTS OF ADENOSINE DEAMINASE INHIBITORS ON LYMPHOCYTE MITOGEN RESPONSIVENESS IN THE MOUSE.

**Ballow M, Pantschenko AG**
**Dept. Pediatrics, Univ. Connecticut Health Center, Sch. Medicine, Farmington, CT, 06032**
**Cell Immunol; 64(1):29-43 1981**

The effects of two adenosine deaminase (ADA) enzyme inhibitors, EHNA (erythro-9-(2-hydroxyl-3-nonyl)adenine) and 2'dCF (2-deoxycoformycin), were examined on mitogen-induced lymphocyte blastogenesis in mice. The proliferative response of spleen cells stimulated with PHA was more sensitive to the inhibitory effect of 2'dCF than was the proliferative response to Con A, 78 and 39% inhibition, respectively. The inhibitory effect increased with increasing concentrations of 2'dCF up to a concentration of 1.0 uM and then plateaued. A dose-related inhibitory effect of EHNA was observed with both PHA and Con A-induced spleen cell mitogenesis. No differences in the susceptibility to EHNA were observed for the two mitogens. EHNA had little inhibitory effect on the LPS-induced mitogenic response of spleen cells. Moreover, at low concentrations of EHNA (0.1-20 uM), an augmentation in the proliferative response to LPS was observed which was eliminated by removing T cells from the spleen cell suspension by treatment with anti-Thy 1.2 and complement. In contrast, 2'dCF produced 50% inhibition at 50 uM concentrations. The effect of these ADA inhibitors was also tested on thymocyte subpopulations separated by peanut agglutination (PNA) and cortisone treatment (CRT). The less mature cortical thymocytes (PNA+) were more susceptible to ADA inhibition by 2'dCF and EHNA than the more mature medullary thymocytes (PNA-, CRT). These results demonstrate that the susceptibility of thymocyte subpopulations to ADA inhibitors changes with different stages of maturation. The spleen cell studies suggest that there are two subpopulations of mitogen responsive T cells, one which is relatively sensitive and the other resistant to the inhibitory effects of 2'dCF. ADA inhibitors, especially 2'dCF, may be useful tools to better define lymphocyte subpopulations and to study lymphocyte differentiation and cellular interactions. (Author abstract) (53 Refs)

## OTHER RELATED STUDIES

### 70. RECEPTOR MEDIATED MURINE LEUKEMOGENESIS: MONOCLONAL ANTIBODY INDUCED LYMPHOMA CELL GROWTH ARREST.

**McGrath MS, Jerabek L, Pillemer E, Steinberg RA, Weissman IL**
**Dept. Pathology, Stanford Univ. Medical Center, Stanford, CA, 94305**
**Haematol Blood Transfus; 26:360-364 1981**

A receptor-mediated leukemogenesis hypothesis that T lymphocytes are clones of T cells bearing mitogen-linked surface receptors specific for the envelope determinants of the inducing murine leukemia virus was tested. Experiments examined the central postulate that continued leukemic proliferation is the result of continued antigenic stimulation of T lymphomas. Monoclonal antibody reagents to leukemia cell surface determinants were raised; the effect of these antibodies was tested on leukemic cell proliferation in vitro and on specific virus binding to the cells. Several antibodies which inhibited lymphoma cell proliferation in vitro were found. Evidence is presented that inhibition may be due to a blockade in virus binding to these cells. (17 Refs)

### 71. T-LYMPHOCYTE SUBPOPULATIONS IN CHRONIC LYMPHOCYTIC LEUKEMIA: A QUANTITATIVE AND FUNCTIONAL STUDY.

**Semenzato G, Pezzutto A, Agostini C, Albertin M, Gasparotto G**
**Clinica Medica 2, Via Giustiniani 2, Padova, Italy**
**Cancer; 48(10):2191-2197 1981**

In the peripheral blood of patients with chronic B-cell lymphocytic leukemia (B-CLL) absolute numbers of E-rosetting lymphocytes were increased. The proportions of TG and TM cell subsets were analyzed, as were their effects on the pokeweed mitogen (PWM)-dependent differentiation of normal allogenic B cells of of autologous leukemic cells. The TG lymphocyte subset was further studied for its cytotoxic activity in antibody-dependent cellular cytotoxicity (ADCC). A marked increase both in percentages and in absolute numbers of TG cells was found. TM lymphocytes percentages were normal, but because of the T lymphocytosis occurring in all patients, the absolute numbers of TM were increased. TM and TG subsets showed helper and suppressor activity, respectively, in PWM-induced B-cell differentiation. TG cells displayed effector cell activity in ADCC. The results provide further evidence that T lymphocytes from patients with B-CLL are functionally normal. However, a noticeable increase of the T-cell subset having suppressor and cytotoxic activity in ADCC was observed. This may be the consequence of a normal immune reaction to the leukemic population. (Author abstract) (45 Refs)

### 72. THE SIGNIFICANCE OF IMMUNOLOGICAL INVESTIGATIONS DURING RADIOTHERAPY FOR BREAST CANCER.

**Boller B, Karcher KH**
**(c/o Karcher) Universitatsklinik fur Strahlentherapie und Strahlenbiologie, Alser Strasse 4, A-1090 Wien, Austria**
**Wien Klin Wochenschr; 93(17):547-551 1981**

Immune response was measured in a group of 50 patients with carcinoma of the bre ast. Factors to be determined included (1) the influence of the tumor on immmunocompetence (IC), (2) the influence of removal of visible tumor on IC, (3) the influence of local irradiation on IC, (4) the influence of other therapeutic measures on IC, (5) indication of tumor recurrence or progression by IC parameters, and (6) indication of the course of disease by changes in IC during therapy. Parameters measured included IgA, IgG, IgM, IgE, lymphocyte migration, lymphocyte membrane fluorescence, T cell rosette formation, granulocyte phagocytosis, and reactions to skin tests. At the time of study 12 patients had died, 20 showed metastases, and 6 showed recurrence of tumor. Results were compared with results for patients with benign tumors and for healthy individuals. No useful clinical methods could be developed for early diagnosis, prognosis, or measurement of disease progress based on immune response. (23 Refs) (In GER)

### 73. DOES PROXIMITY TO COLORECTAL CARCINOMA SUPPRESS THE IMMUNOLOGICAL COMPETENCE OF LYMPHOCYTES? (MEETING ABSTRACT).

**Hutchinson GH, Heinemann D, Symes MO, Williamson RC**
**Department of Surgery, Bristol Royal Infirmary, Bristol, England**
**Gut; 22(5):A422 1981**

The finding that lymphoreticular infiltration of solid tumors may impart a favorable prognosis prompted a study of lymphocyte immunoreactivity in human colorectal cancer. Tumor digests (collagenase/DNAse) from 16 large-bowel carcinomas

were passed through a nylon-wool column to separate neoplastic cells and tumor infiltrating lymphocytes. Lymphocytes were also obtained from the peripheral blood by centrifugation on a Ficoll-Isopaque gradient. The cytotoxicity of each population of lymphocytes was assayed against autoplastic tumor cells, using a two hr 51Cr release assay. In 11 of 16 patients peripheral blood lymphocytes showed moderate cytotoxicity, whereas tumor infiltrating lymphocytes showed similar cytotoxicity in only five cases. The cytotoxicity of tumor infiltrating lymphocytes from 11 patients was therefore compared before and after washing six x in medium 199. Reactivity against tumor cells was shown by unwashed tumor infiltrating lymphocytes in three of 11 and by washed tumor infiltrating lymphocytes in nine (p less than 0.02). At effector: target ratios of 10:1 and 20:1 the level of reactivity was significantly greater for washed tumor infiltrating lymphocytes. The cytotoxicity of lymphocytes derived directly from the tumor may be impaired by a blocking factor (perhaps tumor-associated antigen), adherent to the lymphocyte membrane but removed by washing. Proximity to the carcinoma may suppress the immunological competence of lymphocytes. (no Refs)

## 74. DISTRIBUTION OF HLA CLASS 1 ANTIGENS IN NORMAL HUMAN TISSUES AND MAMMARY CANCER (MEETING ABSTRACT).

McGee JO, Fleming KA, McMichael J, Woods J, Morton J
Nuffield Departments of Pathology and Medicine, University of Oxford, Oxford, England
Br J Cancer; 43(4):564 1981

HLA antigens are glycoproteins which are presumed to be located exclusively on cell surfaces. These antigens are of two classes: Class 1 (HLA-A,B,C) and Class 2 (HLA-DR). It has been assumed from absorption experiments of HLA antisera with whole-tissue homogenates that these antigens are present in virtually all nucleated cells. HLA antigens modulate some cell-mediated immune responses by major histocompatibility complex (MHC) restriction of T-cell-mediated immunity. This is of proven relevance in immunity to viral infections, and may also be relevant to T-cell-mediated responses to tumor cells. In this paper, using monoclonal antibodies it is shown that HLA Class 2 antigens are expressed only on normal lymphoid cells, vascular endothelial, and certain types of epithelial cell (including mammary-duct epithelium). In contrast HLA (A,B,C) antigens are expressed in half of 19 human mammary cancers examined to date. A prospective study is underway to determine whether the expression of HLA Class 1 antigens on human mammary cancer cells is of prognostic significance since the natural history of these tumors is variable. (no Refs)

## 75. LYMPHOID CELLS INFILTRATING HUMAN PULMONARY TUMORS: EFFECT OF INTRALESIONAL BCG INJECTION.

Niitsuma M, Golub SH, Edelstein R, Holmes EC
(c/o Golub), Univ. California Los Angeles Sch. Medicine, 54-140 CHS, Los Angeles, CA, 90024
JNCI; 67(5):997-1003 1981

Tumor-infiltrating lymphocytes (TIL) and regional lymph node lymphocytes (LNL) were isolated by mechanical disaggregation and density gradient centrifugation from 30 untreated human lung tumors and 12 BCG-injected human lung tumors. Lymphocyte populations were characterized by their ability to form erythrocyte (E)-rosettes, RBC-antibody-complement, and RBC-antibody gamma-rosettes, by their proportion of esterase-staining cells, and by their responses in mixed lymphocyte culture (MLC), cell-mediated lympholysis (CML), and natural killer (NK) assays. TIL from untreated tumors had low proportions of E-rosetting cells (mean, 27.3%), relatively high proportions of 'null' cells, and poor responses in MLC-CML and NK assays. There were no significant differences between primary lung tumors and lung metastases in rosettes, MLC-CML responses, or NK activity. In contrast, TIL from tumors injected with BCG 14 days before resection had higher proportions of E-rosetting cells (47.8%) and vigorous MLC-CML and NK responses. LNL from 11 patients with untreated tumors had higher proportions of E-rosetting cells (40.5%) than LNL from 9 patients with BCG-injected tumors (35.0%), and LNL from patients with untreated tumors had higher responses than LNL from treated patients in MLC-CML assays. These results suggest that the BCG injection induced an infiltration of functionally reactive NK and T-cells at the tumor site without an associated increased activity of T-cells from regional lymph nodes. (Author abstract) (32 Refs)

## 76. SUPPRESSOR T-LYMPHOCYTES WITHIN HUMAN COLON CANCER (MEETING ABSTRACT).

Pucci A, Doe WF
Department of Medicine, University of Sydney at Royal North Shore Hospital, St. Leonards, 2065 New South Wales, Australia
Gastroenterology; 80(5,part2):1254 1981

Although peripheral blood studies of cell mediated immunity have been conducted in colon cancer patients, the relevance of these findings to tumor development is unclear. Since suppression of immunity to colon carcinoma represents a potentially important mechanism for tumor growth, the central question is whether suppression of T-cell responses occurs within the cancer itself. Human colon cancers were therefore disaggregated by mechanical means involving mincing, sieving and passage through a glass bead column. The tumor-derived cell suspension was characterized and the constituent cell population separated by bovine serum albumin density gradients to yield fractions enriched for tumor cells, macrophages and lymphocytes. The T-lymphocyte population was purified by sedimentation after rosetting with sheep RBC. Suppressor activity was tested by mitogenic responses to phytohemagglutinin in co-cultures of tumor-derived cells and autologous peripheral blood lymphocytes. In 9 out of 10 separate experiments the tumor-derived cells suppressed the mitogenic response of blood lymphocytes by 30-90%. Fractionation of the tumor disaggregate into T- and non T-cell populations indicated that the suppressor activity was constantly present in the T-cell population. By contrast, the heterogeneous T-cell-depleted population was variable in its effect and on occasion, actually enhanced the response to mitogen. These data establish for the first time the existence of a dominantly suppressor T-cell population within human colon cancers, and encourage further study of the regulation of T-cell responses in this common disease. (no Refs)

## 77. HUMAN THYMOMA: IMMUNOLOGIC CHARACTERISTICS OF THE LYMPHOCYTIC COMPONENT.

Lauriola L, Maggiano N, Marino M, Carbone A, Piantelli M, Musiani P
Dept. Pathology, Universita Cattolica S. Cuore, Via Pineta Sacchetti, 644, 00168 Rome, Italy
Cancer; 48(9):1992-1995 1981

Several immunologic parameters were investigated in the lymphocytic component of 10 thymomas, characterized by a variable degree of lymphocytic infiltration. The majority of thymoma lymphocytes are T-cell in nature, as are lymphocytes from the normal thymus. Lymphocytes from six thymomas

with moderate or predominant lymphocytic infiltrates were capable of forming stable E-rosettes, (mean percentage +- SD: 78.0 +-5.2); binding peanut agglutinin (67.3 +-8.6); and exhibiting receptor for the Fc-porti on of IgM (21.8 +-6.0) at percentages that were close to those found in the normal thymus. On the other hand, lower numbers of stable E-rosetting cells (26.8 +-8.7), PNA-positive cells (27.5 +-12.4), and remarkably higher percentages of cells with receptors for IgM (54.0 +-4.2) were demonstrated by the lymphocytic population of four thymomas with scant lymphocyte components. In addition, lymphocytes from tumors with scant lymphocyte components show a higher proliferative response to phytomitogen (PHA), therefore exhibiting immunologic features comparable to those of the more mature pool of normal medullary thymocytes. The observed immunologic similarities between the populations of lymphocytes from thymomas and from the normal thymus gland suggest an exclusively epithelial origin of the thymoma. (Author abstract) (22 Refs)

## 78. IMMUNOLOGIC MONITORING IN BREAST CANCER PATIENTS RECEIVING POSTOPERATIVE ADJUVANT CHEMOTHERAPY.

**Strender LE, Blomgren H, Petrini B, Wasserman J, Forsgren M, Norberg R, Baral E, Wallgren A**

**Radiumhemmet, Karolinska Hosp., S1-104 01 Stockholm Sweden**

**Cancer; 48(9):1996-2002 1981**

A group of 17 patients, having undergone modified radical mastectomy for breast cancer, received 12 cycles of chemotherapy with methotrexate, 5-fluorouracil, and chlorambucil during 17 mo. The number of circulating T and non T lymphocytes, as defined by E, EAC, and ME rosette formation, were reduced during treatment. The Non-T lymphocytes, however, were reduced to the highest relative extent. Relative phytohemagglutinin and mixed lymphocyte culture responses of the cells decreased, whereas purified protein derivative responses were unchanged. Serum concentrations of IgM were reduced, but IgA and IgG concentrations were unchanged or slightly increased. Antibody titers to morbilli and herpes simplex were not changed, whereas the antibody activity against cytomegalovirus (CMV) increased in several seropositive patients. None of these patients, however, developed signs of a CMV infection. (Author abstract) (37 Refs)

## 79. CHROMOSOME 14 MARKERS IN TWO EPSTEIN-BARR VIRUS (EBV)-TRANSFORMED LYMPHOBLASTOID CELL LINES OF NORMAL ORIGIN DIFFER FROM THE BURKITT LYMPHOMA (BL)-ASSOCIATED 14Q+ MARKER.

**Manolov G, Manolova Y, Klein G, Levan A, Kieler J**

**(c/o Klein) Dept. Tumor Biology, Karolinska Inst., S-104 01 Stockholm, Sweden**

**Cancer Genet Cytogenet; 4(2):179-184 1981**

Two among 10 Epstein-Barr Virus (EBV)-transformed lymphoblastoid cell lines contained a 14q+ marker in a low frequency of the cells (2 and 9%). By means of 'mesome-prosome' analysis of the G-band patterns of these markers; it was established that the additional chromosome segments of these two 14q+ markers came from chromosomes 3 and 5, respectively, and not from chromosome 8 as in the 14q+ marker of Burkitt lymphoma. Chromosome 8 was not involved at all in any changes in the 10 lymphoblastoid cell lines studied. (Author abstract) (19 Refs)

## 80. PHENOTYPIC CHARACTERIZATION IN MICE OF THYMUS TARGET CELLS SUSCEPTIBLE TO PRODUCTIVE INFECTION BY THE RADIATION LEUKEMIA VIRUS.

**Boniver J, Decleve A, Honsik C, Leiberman M, Kaplan HS**

**(c/o Kaplan) Cancer Biology Res. Lab., Dept. Radiology, Stanford Univ. Sch. Medicine, Stanford, CA, 94305**

**JNCI; 67(5):1139-1151 1981**

The spread of virus replication was studied by electron microscopy in the thymuses of inbred C57BL/Ka mice after intrathymic inoculation of the radiation leukemia virus (RadLV). The first Type C-budding virus particles appeared in scarce blast cells of the subcapsular zone. Most of these blast cells were 'X-cells,' ie, the thymus lymphoid cells most actively engaged in DNA synthesis. Virus replication spread to the entire cortical blast cell population and, from Day 7 on, to the small cortical lymphocytes. The first virus-producing cells were derived from a very few target cells (approx 0.001-0.003% of thymocytes) susceptible to RadLV infection. For determination of the phenotypes of these target cells, various thymocyte subpopulations obtained through a battery of cell separation methods were tested for their ability to support the replication of RadLV/VL3 virus in short-term culture. Most of these target cells were sensitive to the lytic effect of hydrocortisone and migrated in the fastest fraction of a 1xG sedimentation gradient, together with the majority of [3H]thymidine-incorporating blast cells. They exhibited an intermediate density and expressed H-2 and Thy 1.2 cell surface antigens, although they were not found preferentially among the high Thy 1.2 population to which most of the cortical blast cells belonged. The spread of RadLV within the thymus and the surface phenotype characteristics of target cells indicate that these cells correspond to a thymocyte subset at the earliest stage of thymic lymphopoiesis and may be transitional between the prothymocytes and the subcapsular blast cell population. (Author abstract) (47 Refs)

## 81. GENETICS OF SUSCEPTIBILITY TO RADIATION-INDUCED LEUKEMIA. MAPPING OF GENES INVOLVED TO CHROMOSOMES 1, 2, AND 4, AND IMPLICATIONS FOR A VIRAL ETIOLOGY IN THE DISEASE.

**Meruelo D, Offer M, Flieger N**

**Irvington House Inst., New York Univ. Medical Center, New York, NY, 10016**

**J Exp Med; 154(4):1201-1211 1981**

The genetics of susceptibility to radiation-induced leukemia in (A/J x B10)F2 mice were defined and the genes involved were localized. A major locus conferring resistance to fractionated irradiation (Cs-137; 180 rad/wk for 4 wk) induction of leukemia was mapped in chromosome 2 (Ril-1). Loci next to xenotropic murine leukemia virus (MuLV) envelope-related cell-surface antigens (XenCSA) on chromosome 4 (Ri 1-3) and Pep-3 on chromosome 1 (Ril-2) also influenced susceptibility to the leukemia. Leukemia incidence on day 250 after last irradiation was 86% and 90% in mice lacking the phenotypes Ly-6.2 or Ly-11.2, respectively, on chromosome 2. Effects related to genes linked to Ly-15.2R and Pep-3 loci were less important: the number of phenotype-nonleukemic animals 300 days after irradiation were 29% (phenotype 15.2/15.2) and 15% (Pep-3 phenotype AA). Ril-1 is located in a chromosomal site rich in thymus differentiation-specific loci; a linkage of Ril-1 and Ly-11 suggests that this region of chromosome is not silent to the inductive effects of fractionated irradiation. Tissue-specific activation of endogenous viruses may be explained by dependency on differentiation-specific steps. (40 Refs)

## 82. GENETIC APPROACHES TOWARD ELUCIDATING THE MECHANISMS OF TYPE-C VIRUS-INDUCED LEUKEMIA.

Aaronson SA, Barbacid M, Dunn CY, Reddy EP
Lab. RNA Tumor Viruses, NCI, Bethesda, MD, 20014
Haematol Blood Transfus; 26:455-459 1981

The mechanisms of induction of leukemia by murine type-C viruses was studied in newborn NIH/Swiss mice. Inoculations of 5 x 10(4) XC pock forming units of either Rauscher (R) or Moloney (M) murine leukemia virus (MuLV) produced gross enlargement of spleen and lymph nodes as early as 10-11 wk. RMuLV produced spleen enlargement and sometimes liver and peripheral or visceral lymph node enlargement. MMuLV produced thymus enlargement in most animals, and frequently affected other lymphoid organs. MMuLV-induced tumors were of T cell origin, as indicated by presence of Thy1 antigen and absence of Fc or C3 receptors. RMuLV-induced tumors were of B cell lineage, as indicated by presence of Fc receptors and absence of Thy1 antigen. Recombinant forms between oncogenic and nononcogenic type-C viruses were produced in wild mouse embryo cells of line WM-C. These recombinants contained genetic information in varying amounts from both parental viruses and exhibited varying degrees of oncogenicity. Results indicate that target cells for transformation by RMuLV and MMuLV contain specific markers distinguishing them from other lymphoid elements. The necessity of active virus replication for tumorigenesis by murine type-C viruses is suggested. (19 Refs)

## 83. THYMIC NURSE CELLS: INTRAEPITHELIAL THYMOCYTE SOJOURN AND ITS POSSIBLE RELEVANCE FOR THE PATHOGENESIS OF AKR LYMPHOMAS.

Kyewski B, Hunsmann G, Friedrich R, Ketelsen UP, Wekerle H
(c/o Wekerle), Max-Planck-Institut fur Immunbiologie, Stubeweg 51, 7800 Freiburg-Zahringen, W. Germany
Haematol Blood Transfus; 26:372-376 1981

Thymic nurse cells (TNCs) are epithelial cells of enormous size which are isolated from normal thymus by differential trypsinization. A study of TNCs from AKR/J mice showed them to be unusual in several respects. TNCs from 3-mo-old mice were abnormally large, with diameter greater than 50-70 micron and containing approx 200 thymocytes in the cell body. TNCs in young adult AKR/J mice resemble those in normal strains. However, as soon as neoplastic conversion occurs (at age 6-8 mo), the number of TNCs drastically declines; none were found in thumus showing signs of neoplasia. TNCs express retroviral products in cytoplasm and membrane. Indirect immunofluorescence using specific conventional antisera and fluorescein-labeled anti-immunoglobulin antibodies as markers demonstrated retroviral products in the epithelial parts of TNCs. The markers viral coat glycoprotein gp71, viral core protein p30, and released viral reverse transcriptase were employed. Although expression of viral determinants on AKR/J cells was unequivocal, TNCs from mouse strains without thymoma predilection also expressed retroviral determinants to a lesser degree. The same was found for the other strains tested, C3H/f and C57BL/6. (16 Refs)

## 84. DETERMINANTS OF SUSCEPTIBILITY AND RESISTANCE TO FELINE LEUKEMIA VIRUS INFECTION. I. ROLE OF MACROPHAGES.

Hoover EA, Rojko JL, Wilson PL, Olsen RG
Dept. Veterinary Pathobiology, Ohio State Univ., 1925 Coffey Rd., Columbus, OH, 43210
JNCI; 67(4):889-898 1981

The role of autochthonous peritoneal feline macrophages (Mtheta) in the age-related resistance of cats to feline leukemia virus (FeLV) was investigated by a study of the functional properties and FeLV susceptibility of Mtheta from kittens and adult cats and the effect of hydrocortisone (HC) and silica on Mtheta-FeLV interactions. Although the phagocytic functions of isolated Mtheta from kittens and adults were equivalent, the mean FeLV susceptibility of Mtheta from kittens was 5x that of Mtheta from adult cats, thus establishing a direct correlation between the age-related susceptibility of cats and Mtheta from cats to FeLV. Mtheta of viremic cats were found to be infected with FeLV in vivo; virus titers were slightly higher than those obtained after in vitro infection of Mtheta. Mtheta from cats that had experienced regressive FeLV infection were not significantly more resistant to FeLV infection in vitro than were Mtheta from naive adult specific-pathogen-free cats. HC, which has been shown to enhance the in vivo FeLV susceptibility of cats, also enhanced the permissiveness of Mtheta from cats to FeLV in vitro (600-fold for Mtheta from adult cats and 200-fold for Mtheta) from kittens. Mtheta permissiveness to FeLV was highly sensitive to HC and occurred in Mtheta infected in vivo or in vitro. In parallel with the effect of HC on the natural resistance of cats to FeLV, administration of silica before virus inoculation also markedly enhanced the FeLV susceptibility of adult cats. Silica was toxic for isolated Mtheta but not for lymphocytes in vitro, and silica produced monocytopenia and neutrophilia, delayed skin allograft rejection, and augmented feline oncovirus-associated cell membrane antigen antibody responses in vivo. These experiments indicate that Mtheta were linked to the natural resistance of cats to FeLV and that the temporary elimination of Mtheta functions (eg, by silica) and/or the conversion of the Mtheta-FeLV relationship from a nonpermissive to a permissive state (eg, by corticosteroids) resulted in failure of early virus containment, in persistent virus amplification in hemolymphatic tissues, and in subsequent FeLV-related proliferative or antiproliferative disease. (Author abstract) (72 Refs)

## 85. DETERMINANTS OF SUSCEPTIBILITY AND RESISTANCE TO FELINE LEUKEMIA VIRUS INFECTION. II. SUSCEPTIBILITY OF FELINE LYMPHOCYTES TO PRODUCTIVE FELINE LEUKEMIA VIRUS INFECTION.

Rojko JL, Hoover EA, Finn BL, Olsen RG
Dept. Veterinary Pathobiology, Ohio State Univ., 1925 Coffey Road, Columbus, OH, 43210
JNCI; 67(4):899-910 1981

The interplay between feline leukemia virus (FeLV) and feline lymphocytes (lc) infected in vitro or in vivo was investigated. Surface marker analysis and viral infectivity (VI) assays of lc populations were used to determine susceptibility of lc subsets to FeLV. The principal FeLV-replicating cell in the mesenteric lymph node of persistently infected, preleukemic cats was a nonadherent, complement receptor (CR)-bearing lc (B-cell). The lymph nodes of preleukemic cats also had increased numbers of uninfected T-cells [cells forming rosettes with guinea pig RBC (GPE)] and cells with receptors for the Fc portion of 7S IgG (FcgammaR cells) as compared with

lymph nodes of age-matched specific-pathogen-free (SPF) cats. The induction of productive infection of feline peripheral blood mononuclear WBC (PBL) in vitro depended on a 48-hr in vitro preincubation period before virus exposure. The equivalent susceptibility of whole and adherent cell-depleted PBL to productive infection and the failure of hydrocortisone to enhance viral infection were compatible with identification of the FeLV-replicating cell as an lc. Furthermore, lc from susceptible SPF kittens replicated 50x as much FeLV as did lc from resistant adult SPF cats. The lc productively infected with FeLV after in vitro exposure were more precisely identified with the use of Ficoll-Isopaque density gradient separation of rosetted and non-rosetted lc. Whole PBL, GPE rosette-positive PBL (T-cells), and CR-positive PBL (B-cells) were permissive to FeLV infection, and max VI was evident at 14 days after exposure. The substantial (1,325-fold) increment in VI found in the FcgammaR-depleted PBL suggested a role for FcgammaR cells in the containment of FeLV infection. Unstimulated mononuclear WBC from blood, spleen, lymph node, thymus, and marrow were susceptible to productive FeLV infection after in vitro exposure. Th e degree of spontaneous DNA synthesis in marrow, thymus, and spleen but not lymph node or PBL was inversely related to permissiveness to viral replication. Mitogen activation of lc was associated with decreased viral replication when either T-cell mitogens (concanavalin A, phytohemagglutinin, or pokeweed mitogen) or a B-cell mitogen (dextran sulfate) was used. Virus production by spleen cells and PBL was enhanced twofold to 10-fold by prior lc stimulation by the B-cell mitogen, lipopolysaccharide, or protein A-bearing Staphylococcus aureus, a mitogen for feline T-cells with FcgammaR. Both productively infected (preincubated) and nonproductively infected (freshly isolated) PBL transferred infectious FeLV to autochthonous peritoneal macrophages (Mtheta); most of the virus in PBL-peritoneal Mtheta cocultures was produced by adherent cells, irrespective of whether the adherent or nonadherent cell population was inoculated originally. (Author abstract) (49 Refs)

## 86. TRANSPLANTABLE LYMPHOID LEUKEMIA OF T CELL TYPE INDUCED BY 7,12-DIMETHYLBENZ[ALPHA]ANTHRACENE (DMBA) IN RAT.

**Gal F, Toth K, Peter I, Sugar J**
**Natl. Oncological Inst., Res. Inst. Oncopathology, Rath Gy. u. 7-9, H-1122 Budapest XII, Hungary**
**Arch Geschwulstforsch; 51(6):509-515 1981**

Development of a transplantable T Type lymphoid leukemia induced by 7,12-dimethylbenz[a]anthracene (DMBA) was reported. Eighty outbred Wistar/H-Riop rats received 25 mg DMBA/kg body wt injected into the caudal vein four times at 8-10-day intervals. Results were measured by hematological histological, cytochemical, and immunofluorescence examinations. Leukemia developed in five rats. Two rats had lymphoid and three had myeloid leukemia. The lymphoid leukemic animals were characterized by raised WBC count, enlarged spleen and liver, and massive lymphoid cellular infiltration of the liver, spleen, thymus, bone marrow, lymph nodes, and salivary glands. The leukemia apparently was induced by DMBA, since spontaneous leukemias are relatively rare in rats. T cell origin was indicated by the absence of B-lymphocyte markers, the presence of Thy-1 surface antigen, and cytoplasmic acid phosphatase activity. The leukemia has been maintained in 186 passages with an inoculation take of 96% using a dose of 6 x 10(4) cells/inoculation. Both the myeloid and lymphoid leukemias should be useful in screening of cytostatic drugs for myelotropic or lymphotropic activity. (24 Refs)

## 87. SUBFRACTIONATION OF MALIGNANT VARIANTS OF METASTATIC MURINE LYMPHOSARCOMA CELLS BY COUNTERCURRENT DISTRIBUTION IN TWO-POLYMER AQUEOUS PHASES.

**Miner KM, Walter H, Nicolson GL**
**(c/o Nicolson) Dept. Tumor Biology, Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., Houston, TX, 77030**
**Biochemistry; 20(21):6244-6250 1981**

The low metastatic murine lymphosarcoma parental cell line RAW117-P and a high m etastatic subline (RAW117-H10), selected sequentially 10x for liver colonization, were grown in suspension and subjected to countercurrent distribution (CCD) in a dextran-poly(ethylene glycol) aqueous phase system having an electrostatic potential difference between the phases. Both the RAW117-P and the RAW117-H10 sublines gave broad distribution curves, with the mean partition coefficient of RAW117-H10 cells being higher than the mean partition coefficient of RAW117-P cells. RAW117-P cells were kept in culture over a 2-mo period during which time the mean partition coefficients increased. Concomitant with their in vivo drift in partition coefficients, the RAW117-P cells also displayed increasing heterogeneity as evidenced by the appearance of broader and even multipeaked CCD curves. However, the mean partition coefficients always remained lower than that of the RAW117-H10 subline. Cells from different cavities along the extraction train following CCD of the RAW117-P line were placed into tissue culture, allowed to double overnight, and assayed in vivo by injection of 5 x 10(3) cells iv into BALB/c mice. After 20 days, the RAW117-P cells which had the higher partition coefficients (corresponding more closely to the higher mean partition coefficient of the high metastatic RAW117-H10 subline) formed significantly more liver tumor colonies than did the RAW117-P cells with lower partition coefficients. Analysis of surface proteins on the CCD subfractionated RAW117-P cells by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and staining with 125I-labeled concanavalin A indicated that the cell-surface glycoproteins of the more metastatic cell subpopulations had a decrease in an approx 70,000 mol wt component similar to the highly metastatic subline RAW117-H10. These results suggested that malignant cell variants exist in the parental RAW117-P population and that they can be separated from the majority of cells of low malignant potential by countercurrent distribution. (Author abstract) (34 Refs)

## 88. ACTIVATION OF HUMAN NATURAL KILLER CELL ACTIVITY BY DIFFERENT TYPES AND COMBINATIONS OF HUMAN INTERFERONS (MEETING ABSTRACT).

**Weigent DA, Langford MP, Stanton GJ**
**The University of Texas Medical Branch, Galveston, TX**
**Third International Symposium on Human Lymphokines, October 15-17, 1981, Dallas, Texas Wadley Institutes of Molecular Medicine; 1981**

Human immune (gamma), WBC (alpha) and fibroblast (beta) interferons (IFN) were tested alone or in combination for their capacity to enhance the spontaneous cytoxicity of human peripheral lymphocytes for xenogeneic and allogeneic target cells. All three types of IFN were shown to enhance the cytotoxicity of human natural killer (NK) cells in vitro. IFN-gamma activated natural killing faster and was 100 x more active per unit of antiviral activity then alpha and beta IFN. Combinations of IFN-alpha and IFN-be ta had an additive effect, while combinations of IFN-gamma and alpha or beta IFN were synergistic. The population of cells showing enhanced killing for both mouse L and human K-562 target cells

by IFN-gamma did not absorb to nylon wool and formed rosettes with sheep RBC. Specific antiserum to IFN-gamma added to the IFN preparations, neutralized the enhanced cytotoxic activity by IFN-gamma. The data indicate that human IFN-gamma alone or in combination with alpha or beta IFN could have much greater value for treatment of virus infections or neoplasia where NK cell mediated cytotoxicity is an important host defense. (no Refs)

## 89. LYMPHOCYTES MAINTAINED IN T-CELL GROWTH FACTOR (INTERLEUKIN 2) SHOW ENHANCED CYTOTOXICITY FOR HUMAN TUMOUR CELLS (MEETING ABSTRACT).

Vose BM, Moore M
Christie Hospital and Holt Radium Institute, Manchester M20 9BX, England
Br J Cancer; 43(5):724 1981

Conditions for the production of supernates from mitogen-stimulated human lymphocytes with the capacity to induce proliferation in long-term mixed lymphocyte culture (MLC) or phytohemagglutinin (PHA) cultures which do not respond to PHA have been investigated. These supernates can be used to maintain lymphocytes in continuous growth with a doubling time of approx 48 hr. Cells grown from MLC-stimulated cultures show greater than 80% sheep RBC-rosetting cells, are Fc-, do not show antibody dependent cellular cytotoxicity activity and have reduced lysis of K562 compared with freshly isolated effectors. Cultured T cells (CTC) show high lytic activity against the inducing PHA blasts but not against autologous or third-party targets. Similar experiments have been performed with lymphocytes from the blood, lymph node, spleen and tumor of cancer patients, and CTC tested for cytotoxicity against autologous and allogeneic tumor cells and the K562 cell line. Cytotoxicity for autologous tumor was found in all samples. This was accompanied by killing of allogeneic cells in most instances, but killing of K562 was only rarely demonstrable. These data would be consistent with a polyclonal expansion of cytotoxic effectors in the samples. The finding of autologous reactivity suggests the presence of autorecognitive cytotoxic T cells in cancer patients with specificity for tumor. (no Refs)

## 90. PLASMA MEMBRANE VESICLES AS MEDIATORS OF INTERACTIONS BETWEEN TUMOR CELLS AND COMPONENTS OF THE HEMOSTATIC AND IMMUNE SYSTEMS (MEETING ABSTRACT).

Gasic G, Gasic T
Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, PA, 19140
Chesapeake Conference on Hemostasis and Malignancy-Interaction of Platelets and Tumor Cells, June 26-30, 1981, St Mary's Maryland American Red Cross; 1981

Cells from a variety of mouse and rat tumors can shed plasma membrane vesicles. In vitro experiments indicate that these vesicles can interact with blood platelets and macrophages. Here we report species differences affecting platelet-vesicle interactions and the effects of new compounds on these interactions. Also we raise the hypothesis that vesicle surface material active in platelet aggregation (PA) might also influence immunogeneticity of tumors via vesicle-macrophage interactions. In the rat system, addition of vesicles to platelet rich plasma regularly induce PA. This phenomenon is preceded by binding of vesicles to platelets. Decomplementation blocks both binding and PA. Coumadin reduction of clotting factors and thrombin inhibitors inhibit PA but not binding. In mice, which are widely used as experimental model in thrombogenesis, metastasis, and tumor immunity, platelet responses to vesicles are less predictable and depend on genetic factors affecting complement, clottability, platelet receptors, or a combination of these factors. PA in mice can be fully inhibited in vitro and in vivo by synthetic anti-thrombin compounds and by invertebrate salivary gland extracts. In a syngeneic system, vesicles from a highly immunogenic tumor interacted with macrophages which upon injection into mice enhanced their resistance to sbc tumor grafts. This observation led us to reexamine unpublished data which show a good correlation between tumor immunogenicity and PA activity. It remains to be established whether vesicles released by circulating or invading tumor cells can also successfully interact in vivo with macrophages and which role platelets may play in this interaction. (1 Ref)

☆ U. S. GOVERNMENT PRINTING OFFICE : 1982—361-847/113

# AUTHOR INDEX WITH CITATION NUMBERS


Aaronson SA 82
Abdulkadyrov KM 4
Abe E 62
Abramson CS 18
Agnelli G 30
Agostini C 71
Albertin M 71
Alexander P 63
Andersen C 33
Andre C 15
Aur RJ 6
Bailey J 57
Ballow M 69
Baral E 78
Barbacid M 82
Barel M 39
Bernadou A 29
Beverley PC 51
Blackstock R 8
Blatt J 19
Blomgren H 78
Bloomfield CD 18
Boller B 72
Bollum FJ 13
Boniver J 80
Borowitz MJ 45
Bowman WP 6
Bratescu A 42
Brunning RD 18
Burgess D 57
Caligaris Cappi 11
Callard RE 51
Carbone A 77
Castleberry RP 24
Catovsky D 9
Char DH 44
Charriaut C 39
Clarkson B 32
Clavell LA 10
Coccia PF 18
Cooper MD 8
Costello C 9
Crist WM 24
Crist WM 8
D'Agay MF 15
D'Angona JL 36
De Salazard MD 28
De Salvo Cardul 9
DeBoer KP 42
Dearth JC 24
Decleve A 80
Delia D 13
Delia D 3
Department of H 38
DiPersio L 48
Dilley J 20
Dillman RO 35
Dmoszynska-Gian 21
Dobbie D 63
Doe WF 76
Dowell B 8
Dowell BL 45
Dowell BL 5
Dunn CY 82
Dworkin J 46
Edelstein R 75
Edwards PA 13
Epstein MA 52
Epstein MA 53
Evans DL 57
Falletta JM 8
Fellous M 23
Finn BL 85
Fleming KA 74
Flieger N 46
Flieger N 81
Flint A 24
Forbes P 63
Forsbeck K 55
Forsgren M 78
Fox RI 20
Frade R 39
Freidzon VA 4
Friedrich R 83
Fukuda M 58
Fukuda M 64
Gajl-Peczalska 18
Gal F 86
Gal'perina Ilu 4
Galton D 9
Ganeshaguru K 9
Gasic G 90
Gasic T 90
Gasparotto G 71
Gavosto F 11
George FW 5
Gerber M 68
Geurts van Kess 43
Gidlund M 55
Godal T 54
Goldfarb S 31
Goldstein G 13
Goldstein G 3
Golub SH 75
Good RA 41
Graf IA 17
Greaves M 3
Greaves MF 13
Greaves MF 50
Greaves MF 7
Gresele P 30
Griffin JD 49
Griffiths JC 35
Grover WH 57
Hagemeijer A 43
Hale AH 57
Hamburger AW 2
Hansen MM 33
Hariri G 3
Harris D 57
Heikkila R 54
Heinemann D 73
Henderson ES 14
Henriksen A 54
Hirt A 26
Hoffbrand V 9
Holmes EC 75
Honsik C 80
Hoover EA 84
Hoover EA 85
Hou-Jensen K 33
Hsu C 42
Humphrey GB 8
Hunsmann G 83
Hutchinson GH 73
Idel'son LI 17
Ievleva ES 17
Imbert M 15
Ip S H 56
Izotova TA 16
Jager G 59
Jerabek L 70
Jones NH 45
Jones NH 5
Kagan E 67
Kaplan HS 22
Kaplan HS 80
Karcher KH 72
Kelly DR 24
Kemshead J 3
Kersey JH 18
Ketelsen UP 83
Kharchenko MF 4
Khodzhakulieva 4
Kieler J 79
Kikutani H 41
King MA 34
Kishimoto T 66
Klein G 37
Klein G 79
Kleinman R 42
Klock JC 36
Koeffler HP 58
Konno K 62
Kung P 13
Kung P 3
Kuribayashi T 62
Kyewski B 83
Lachman LB 5
Langford MP 88
Lau B 59
Lauriola L 77
LeBien TW 18
Lebman D 56
Leiberman M 80
Lenskaia RV 16
Levan A 79
Levy R 20
Lewis JC 57
Linch D 51
Lindmo T 54
Luis J 40
Macher BA 36
Macy ML 2
Maggiano N 77
Manolov G 79
Manolova Y 79
Marcilla AG 28

Marino M. 77
Marton PF 54
Matera L. 11
Mauer AM. 6
Mayer EP. 42
McGee JO. 74
McGrath MS. 70
McKenna RW. 18
McMichael AJ. 53
McMichael J. 74
Melvin SL. 12
Melvin SL. 6
Merino F. 40
Mertelsmann R. 32
Meruelo D. 46
Meruelo D. 81
Meserve BL. 35
Metzgar RS. 45
Metzgar RS. 5
Metzgar RS. 8
Meydrech EF. 8
Michael JG. 48
Miller K. 67
Miner KM. 87
Minowada J. 1
Minowada J. 58
Mirchandani I. 31
Miyaura C. 62
Moiseeva VP. 4
Moore M. 89
Moore MA. 32
Morell A. 26
Morilla R. 9
Morstyn G. 47
Morton J. 74
Moss DJ. 52
Moss DJ. 53
Musiani P. 77
Nadler LM. 49
Navas Palacios. 28
Negoro S. 14
Nelson R. 42
Nenci GG. 30
Nesbit ME. 18
Newman RA. 50
Nicolson GL. 87
Nilsson K. 55
Nilsson K. 65
Niltsuma M. 75
Nishii Y. 62
Norberg R. 75
Notis-McConarty. [illegible]
Novarino A. 11
O'Brien M. 9
Offer M. 46
Offer M. 81
Olsen RG. 84
Olsen RG. 85
Pallares MA. 28
Pałatke M. 31
Panetti M. 57
Pang EJ. 42
Panischenko AG. 69
Paolino A. 46
Parise P. 30
Paulus LK. 57
Perussia B. 56
Pesando JM. 10
Pesce AJ. 48
Peter I. 86
Petrini B. 78
Pezzutto A. 71
Piantelli M. 77
Pillemer E. 70
Pivnik AV. 17
Plesner T. 33
Poplack DG. 19
Powles R. 63
Pucci A. 76
Pullen DJ. 8
Ragab AH. 24
Ralfkiaer E. 33
Ralph P. 66
Rand N. 44
Rao J. 3
Reaman G. 19
Reddy EP. 82
Reinherz EL. 60
Rickinson AB. 52
Rickinson AB. 53
Ritz J. 10
Ritz J. 13
Ritz J. 49
Robinson JB. 13
Rojko JL. 84
Rojko JL. 85
Roper M. 24
Rovera G. 56
Royston I. 35
Rozanova LM. 4
Ruebush MJ. 57
Rumiantsev AG. 16
Rupniewska ZM. 21
Ruud E. 54
Rybakova LP. 4
Sallan SE. 10
Sallstrom J. 55
Samochatova EV. 16
Samuskevich IG. 4
Schlossman S. 13
Schlossman SF. 10
Schlossman SF. 49
Schlossman SF. 60
Semenzato G. 71
Seon BK. 14
Serrou B. 68
Sieff C. 13
Sitia R. 41
Smets LA. 43
Stanton GJ. 88
Stavnezer J. 41
Steen HB. 54
Stein H. 25
Stein PC. 44
Steinberg RA. 70
Strauchen JA. 27
Strender LE. 78
Suda T. 62
Sugar J. 86
Sultan C. 15
Sundstrom C. 55
Sutherland DR. 50
Sutherland R. 3
Symes MO. 73
Tabaczka P. 31
Tanaka H. 62
Teodorescu M. 42
Ter-Grigorov VS. 17
Tikhonova LIu. 17
Toth K. 86
Toth SR. 61
Totterman T. 55
Totterman TH. 65
Trinchieri G. 56
Tursz T. 23
Ushakova EA. 4
Vadas MA. 47
Valdes MD. 28
Van Eys J. 8
Van Rooy H. 43
Venge P. 55
Verbi W. 3
Vogler LB. 8
Vose BM. 89
Wallace LE. 52
Wallace LE. 53
Wallgren A. 78
Walter H. 87
Wasserman J. 78
Weigent DA. 88
Weiss MA. 48
Weissman IL. 70
Wekerle H. 83
Wells JV. 34
Wen CM. 42
White CP. 2
Whittingham S. 47
Wiels J. 23
Williamson RC. 73
Wilson JW. 47
Wilson PL. 84
Woods J. 74
Yoshizaki K. 14
Zeuthen J. 37
Zipf TF. 20

# CANCER INFORMATION? CANCERLINE·CANCERLINE·CANCERLINE·

# NOW

## Your Complimentary Copy of

# The Latest DIRECTORY OF CANCER RESEARCH INFORMATION RESOURCES

*Just Return the Form at the Bottom of this Page*

This Directory is Your Guide to the Following Information Sources:

COMPUTERIZED CANCER INFORMATION available through biomedical libraries

PRIMARY JOURNALS containing cancer-related articles

SECONDARY PUBLICATIONS such as abstract bulletins, indexes, bibliographies, etc.

INFORMATION ON PROJECT DESCRIPTIONS AND FUNDING SOURCES

ORGANIZATIONS that provide fellowships, grants, and other support of cancer research, as well as organizations that conduct research

REGISTRIES of cancer patient data

LIBRARIES with special collections of cancer-related literature

CLASSIFICATIONS used to categorize and index cancer information

SPECIAL COLLECTIONS of cancer-related materials

AUDIOVISUAL MATERIALS dealing with cancer

---

Request for **COMPLIMENTARY DIRECTORY:**
(*Print Clearly* for use as mailing label)

Name: _____

Address: _____

_____

City/State/Zip: _____

Country: _____

*Mail to:*
Directory Request
ICRDB Program
National Cancer Institute
Westwood Building Room 10A18
Bethesda, Maryland 20205

## The Latest International Compilation

# PHASE II / PHASE III CLINICAL TRIALS

IN CASE YOU MISSED IT, THE 1981 COMPILATION OF CANCER THERAPY PROTOCOLS IS NOW AVAILABLE

Clinical oncologists are probably familiar with the annual

**Compilation of Cancer Therapy Protocol Summaries**

This volume summarizes clinical trials of:

- new agents
- new techniques
- new combinations of modalities and agents

The Compilation includes nearly 1,500 Phase II and Phase III trials currently in progress in countries around the world. This information is compiled by the International Cancer Research Data Bank--a program of the National Cancer Institute. It is available to you, without charge, as a public service of the program.

## FOR A COMPLIMENTARY COPY, WRITE:

(*Print Clearly* for use as mailing label)

Name: _____

Address: _____

_____

City/State/Zip: _____

Country: _____

Mail to:

**Compilation Request**
ICRDB Program
National Cancer Institute
Westwood Building Room 10A18
Bethesda, Maryland 20205

**U.S. DEPARTMENT OF COMMERCE**
**National Technical Information Service**
5285 Port Royal Road
Springfield, Va. 22161

OFFICIAL BUSINESS

Penalty for Private Use, $300

**PRINTED MATTER**

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF COMMERCE
COM-211

THIRD CLASS
BULK RATE

U.S. MAIL

CB-17

**CANCERGRAMS** are distributed for the International Cancer Research Data Bank (ICRDB) by the National Technical Information Service (NTIS). **CANCERGRAMS** are available from NTIS on a standing order basis at $2 each for North American Continent addressees and $3 each for other addressees. An NTIS deposit account is required. For a list of subject categories or other information, please write to:

Subscription Section
National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161

**NOTICE OF MAILING CHANGE**

☐ Check here if you wish to discontinue receiving this publication.

☐ Check here if your address has changed and you wish to continue receiving this publication. (Be sure to furnish your complete address including zip code.)

Tear off cover with address label still affixed and send to:

Computer Support Center
ICRDB Program
IIT Research Institute
10 West 35th Street
Chicago IL. 60616

CB 17/82/04

NCI/ICRDB/CB17 82/04

PB82-931904

ICRDB

CANCERGRAM

# IMMUNOBIOLOGY AND CANCER

## Identification and Characterization of Immune Cells

SERIES CB17 No. 82/04

APRIL, 1982

This Cancergram is a service of the INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM of the U.S. National Cancer Institute. Every few weeks, an updated Cancergram containing abstracts of selected cancer-related articles recently published in more than 3000 journals, and dealing with the topic indicated by the above title, is sent to researchers working in this area. These researchers are identified on the basis of the description of their current research project that has been submitted to the ICRDB Program, directly or via granting agencies.

This Cancergram is prepared by the Cancer Information Dissemination and Analysis Center (CIDAC) for Virology, Immunology, and Biology. ***If this Cancergram is useful and valuable, please send your comments to the CIDAC address below, since future editions depend on user satisfaction and user needs:***

CIDAC FOR VIROLOGY, IMMUNOLOGY, AND BIOLOGY
SCIENCE INFORMATION SERVICES
FRANKLIN INSTITUTE RESEARCH LABORATORIES
20TH AND RACE STREETS
PHILADELPHIA, PA 19103

NEWARK PUBLIC LIBRARY

APR 29 1982

U. S. GOVT. PUBS.
DEPOSITORY 376

AVAILABLE: DIRECTORY OF CANCER RESEARCH INFORMATION RESOURCES, 1981 EDITION. FOR A COMPLIMENTARY COPY, CONTACT ICRDB PROGRAM, WESTWOOD BLDG., RM. 10A18, BETHESDA, MD. 20205

*In this issue:*


- **CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS..... 1-19**
- **DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS..... 20-26**
- **LYMPHOCYTE AND DIFFERENTIATION ANTIGENS..... 27-34**
- **CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION..... 35-43**
- **EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS..... 44-58**
- **OTHER RELATED STUDIES..... 59-73**


**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Public Health Service • National Institutes of Health • National Cancer Institute**

HE 20.3173/2:

## CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS

### 1. USE OF IMMUNOLOGICAL METHODS IN CHARACTERIZING ACUTE LYMPHOBLASTIC LEUKEMIAS IN CHILDHOOD.

Cap J, Babusikova O, Misikova Z, Foltinova A

II. Detska klinika, Detska fakultna nemocnica, Duklianska 14, 881 25 Bratislava, Czechoslovakia

Bratisl Lek Listy; 76(2):183-191 1981

Spontaneous and immune rosette tests were performed in 47 children (3-14 yr old) with acute lymphoblastic leukemia (ALL). The tests were performed at the time of diagnosis in 26 cases, a nd during complete remission in the course of cytostatic therapy in 21. Immunological classification of ALL was possible in 16 cases: null cell type was found in 10 cases, B cell type in 2, T cell type in 1, and T + B cell type in 3. During the 4-30-mo follow-up period there were no differences in the course of the disease between the individual immunological types. Repeated rosette tests showed normalization of the T and B lymphocyte counts shortly after remission had been achieved. In the further course, the T cell count tended to decrease, reaching normal levels only after completion of the cytostatic therapy, while the B cell count remained within the normal range. (20 Refs) (In SLO)

### 2. SUBCLASSIFICATION IN ACUTE LYMPHOBLASTIC LEUKAEMIA: ACID PHOSPHATASE REACTION AND IMMUNOLOGICAL MARKERS IN RELATION TO CLINICAL FEATURES. A COMPARATIVE STUDY OF 44 PATIENTS.

Boesen AM, Ellegaard J, Hokland P, Lassen BL

Medicinsk-haematologisk afdeling, Aarhus Amtssygehus, DK-8000 Aarhus C, Denmark

Scand J Haematol; 27(2):87-98 1981

A prospective, comparative study of cytochemical and immunological markers and clinical features was undertaken in 44 patients with ALL (children and adults). Twelve patients (27%) had T-ALL, 1 patient (2%) B-ALL and 31 patients (71%) (non-T,non-B)-ALL. E-rosetting lymphoblasts ranged from 35 to 96% (median: 61), highest when AET-treated SRBC were used as indicator cells. All 12 E-rosette positive cases were strongly acid phosphatase (AcP)-positive, showing a homogeneous pattern of distinct granular AcP-activity in more than 85% of the lymphoblasts (median: 96%) significantly different from the median of 26% granulated blasts found in the (non-T, non-B)-ALL cases. Counting blasts with granular AcP-activity proved to be both easier than using a scoring system for the AcP-reaction and more efficient in terms of discriminating ability between the subgroups. Significant clinical and hematological features characterizing the T- and AcP-positive cases included: (1) Predominance of young adult men, (2) presence of a mediastinal mass, (3) involvement of skin and serous membranes, (4) only slightly affected hemoglobin concentration at presentation, (5) difficulty in obtaining complete remission, (6) shorter duration of first complete remission and (7) shorter survival rate. It is confirmed that AcP-staining of lymphoblasts is an easy, reproducible and inexpensive method for identifying the T-cell variety of ALL. (Author abstract) (31 Refs)

### 3. IMMUNOLOGICAL STUDIES IN CHRONIC LYMPHOCYTIC LEUKEMIA. I. ELUCIDATION OF SUBSET HETEROGENEITY.

Hokland P, Ellegaard J

Med. afd. II, Aarhus Amtssygehus, 8000 Aarhus C, Denmark

Leuk Res; 5(4/5):341-348 1981

The B lymphocyte subsets in chronic lymphocytic leukemia (CLL) were examined by three different approaches: rosette sedimentations, double marker assays, and separation of CLL cells according to their densities in continuous Percoll gradients. A hypothesis of sequential alterations of the surface receptor in CLL is presented. RBC and mouse rosette tests yielded complementary results when 30 untreated CLL patients (43-81 yr old) were compared with 10 normal donors. The most stable marker of the malignant B cells was their ability to form rosettes with mouse RBC, while surface membrane immunoglobulins, IgG constant fragment-, and complement receptors were present only on a minor proportion of CLL cells. Lymphocytes forming rosettes with S-aminoethyl-iso-thiouronium bromide-treated sheep RBC were separated from non-rosette forming cells in eight patients; a very high percent of T cells were active RBC-rosette formers. When cells harvested from the non-T fractions were tested for mouse rosette formation, it was found that mouse rosette separation procedures are not as effective as those using sheep RBC: 22% of the cells harvested from the second interface were still able to form mouse rosettes. Double markers were found in 5/5 untreated patients. The surface marker phenotype of large cells, which are frequently seen in CLL patients, was determined. The results indicated considerable heterogeneity in CLL lymphocyte subsets. (25 Refs)

### 4. DIFFERENTIATION ABILITY OF THE CLL LYMPHOCYTE: AN IMMATURE LYMPHOCYTE OR AN ABNORMAL LEUKEMIC CELL?

Dighiero G, Bodega E, Binet JL, Lajtha L, Sachs L, Seligmann M, McCulloch EA, Revoltella, Greaves MJ

Department d'Hematologie, Groupe Hospitalier Pitie-Salpetriere, ERA-CNRS 500, 75013 Paris, France

Blood Cells; 7(2):331-339 1981

Patterns of cell differentiation in chronic lymphocytic leukemia (CLL) are discussed. While most cases of CLL correspond to B-cell disease, a few cases are clearly defined as T-cell proliferations and increasing numbers of null cases have been published. Distinctive features of B-cell CLL lymphocytes include: very low levels of monoclonal surface immunoglobulin; presence of receptors for mouse RBC; and presence of dual B and T markers in a high percentage of cases. The relatively rare T-cell CLL is defined by a characteristic clinicel and hematological picture including presence of receptors for sheep RBC, reactivity with anti-T sera, and negative or very low values of terminal transferase. There is less agreement in findings on the very rare null-cell CLL; more sensitive methods of study may be needed to establish it as an entity. While great progress has been made in the understanding of CLL, two questions remain unresolved: (1) Does the proliferating clone correspond to an immature B-lymphocyte, or does it merely represent an abnormal leukemic cell? (2) What is the role of T cells in B-cell CLL? (40 Refs)

## 5. UNUSUAL T-CELL PHENOTYPE IN ADVANCED B-CHRONIC LYMPHOCYTIC LEUKAEMIA.

Matutes E, Wechsler A, Gomez R, Cherchi M, Catovsky D
(c/o Catovsky) M.R.C. Leukemia Unit, Royal Postgraduate Medical Sch., Hammersmith Hosp., Ducane Road, London W12 0HS, England
Br J Haematol; 49(4):635-642 1981

T-lymphocytes isolated by E-rosetting from 22 patients with B-cell chronic lymphocytic leukemia (B-CLL) showed membrane phenotype features distinct from those of normal T-lymphocytes. These changes were particularly marked in advanced disease (Rai Stages II, III, IV and WBC over 100 x 10(9)/l). The most significant finding was the demonstration, in 10 cases, of a major population of E-rosette positive cells (40-80%) unreactive with the OKT monoclonal antibodies against mature or immature T-cells; 15-30% of the cells were unreactive in 7 other cases. A significant reduction in OKT4 positive (helper) lymphocytes was seen in 18 cases. The proportion of OKT8 positive cells was increased in two and normal or low in the rest. Only four patients with early disease (Stages 0 and I) had a normal T-cell phenotype. These findings could explain abnormalities previously described in the T-lymphocytes of B-CLL and provide new insights into the pathogenesis of the disease. (Author abstract) (19 Refs)

## 6. T-CELL CHRONIC LYMPHOCYTIC LEUKEMIA.

Gopal R, Advani SH, Nair CN, Dinshaw KA, Nadkarni JJ, Satam MN, Gawande SR, Sirsat SM
Dept. Medicine and Haematology, Tata Memorial Hosp., Parel, Bombay 400 012, India
Tumori; 67(5):405-410 1981

A case of T-cell chronic lymphocytic leukemia (T-CLL) is reported. The surface receptor for sheep RBC and acid phosphatase staining confirmed the diagnosis of T-CLL. This report provides evidence that T-CLL, a rare variant of CLL, is an aggressive disease with relative resistance to therapy and short survival. (Author abstract) (32 Refs)

## 7. PH(1)-NEGATIVE T LYMPHOCYTIC COLONIES IN AGAR CULTURES OF PERIPHERAL BLOOD IN CHRONIC MYELOID LEUKEMIA.

Bagnara GP, Biagini G, Marani M, Bonsi L, Severi B, Valvassori L, Comis M, Nobile F, Iacopino P, Ronco F, Neri A
Instituti di Isotologia ed Embriologia Generale e, Universita di Bologna, Italia
Acta Haematol (Basel); 66(3):174-180 1981

T lymphocytic colony formation by peripheral lymphocytes separated by discontinuous albumin gradient centrifugation was evaluated in eight patients with Philadelphia (Ph(1))-positive chronic myeloid leukemia (CML). Colonies were obtained using a liquid-on-agar culture system recently introduced (PHA overlayer-WBC feeder layer assay) which has been shown to be simple and reliable. The pattern of colony growth in CML and in normal controls was similar, the peak ranging from the 4th to the 6th day. Also the morphological aspects of colonies did not differ in the two groups. Cells recovered from CML lymphocytic colonies were shown to belong to T cell lineage, as they are able to form spontaneous E-rosettes and to respond to mitogenic stimulation in vitro. In contrast, cells recovered from all other cultured fractions failed to display these properties. Cytogenetic analysis showed that T colony cells were Ph(1)-negative whereas the chromosome anomaly was found in nonlymphoid colonies of the same patients, thus suggesting a nonclonal origin of T lymphocytes in CML. (Author abstract) (25 Refs)

## 8. SEVERAL MARKER ANALYSES OF T-LYMPHOMA CELLS IN EIGHT JAPANESE ADULTS.

Nasu K, Tatsumi E, Takiuchi Y, Kita K, Nishikori M, Shirakawa S, Uchino H
First Div. Internal Medicine, Faculty Medicine, Kyoto Univ., Sakyo-ku Kyoto 606, Japan
Am J Clin Pathol; 76(5):670-678 1981

Lymphoma cells in eight adult Japanese patients with no evidence of overt leukemia throughout their clinical course were demonstrated to be of T-cell nature by combining studies of various immunologic cell surface markers and cytochemistry. The histologic diagnosis of these patients was diffuse histiocytic lymphoma in four patients, poorly differentiated lymphocytic lymphoma in two patients and mixed histiocytic and lymphocytic lymphoma in two patients, according to Rappaport's classification. In seven of the eight patients, the malignant appearance and the large number of E-rosetting cells readily led to the diagnosis of T cell lymphoma. Human Ia-like antigens were unexpectedly detected on the malignant T cells in seven of the eight patients. TdT activity was elevated in two of the four patients tested. Acid phosphatase activity was always observed in the neoplastic T-cells, and this activity was tartrate resistant. Focal activity of acid alpha-naphthyl acetate esterase was detected in the malignant cells with somewhat mature appearances, but large immature cells had no or weak dispersed activity. Except for E-rosetting ability, malignant T-cells showed such variable properties that multiple marker analyses seem to be necessary in the diagnosis and the prediction of prognosis of these disorders. Frequent occurrence of T-cell malignancy in Japan was also discussed. (Author abstract) (52 Refs)

## 9. PHENOTYPIC HETEROGENEITY AND CELLULAR ORIGINS OF T CELL MALIGNANCIES.

Greaves MF, Rao J, Hariri G, Verbi W, Catovsky D, Kung P, Goldstein G
Membrane Immunology Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England
Leuk Res; 5(4/5):281-299 1981

The reactivity of the OKT series of monoclonal antibodies was compared with a panel of other monoclonal antibodies, sheep erythrocyte rosette formation, and expression of terminal deoxynucleotidyl transferase in untreated T cell malignancies. Also included in the series were OKT11 and OKT11A, two new monoclonal antibodies with pan-T activity. The composite phenotypes of cells from individual patients were classified according to a presumptive sequence of T lymphocyte differentiation. Six categories of T cell phenotypes were designated, four of thymic type and two of mature T cells. Cells from 82 untreated patients with T cell malignancy were tested with the OKT series of monoclonals and other markers. The OKT defined phenotype of 13 established T cell lines is presented. The most striking result from this analysis was the association between overall phenotype and diagnostic subgroup of T cell malignancy. The results indicated that T cell leukemias have exclusive, composite phenotypes which are in themselves remarkably heterogeneous. It was suggested that T-cell acute lymphoblastic leukemia and T-cell non-Hodgkin's lymphoma in young patients originate in a thymic stem cell with varying levels of maturation arrest, whereas those T malignancies in adults with a mature T cell phenotype arise from long-lived immunocompetent T cells. (79 Refs)

## 10. MALIGNANT LYMPHOMA WITH DUAL B AND T CELL MARKERS. ANALYSIS OF THE NEOPLASTIC CELLS WITH MONOCLONAL ANTIBODIES DIRECTED AGAINST T CELL SUBSETS.

Aisenberg AC, Bloch KJ, Wilkes BM
Huntington Memorial Lab., Massachusetts General Hosp., Boston, MA, 02114
J Exp Med; 154(5):1709-1714 1981

A human malignant lymphoma with characteristics of both B and T cells is reported. Neoplastic lymphocytes from five patients were analyzed. B cell characteristics were indicated by demonstration of surface-bound immunoglobulin containing IgM heavy chains and kappa light chains, an Ia-like antigen, and complement receptors. T cell characteristics were indicated by reaction with monoclonal antibodies for detection of sheep RBC OKT11 receptors (all cases), normal peripheral blood T cell OKT 3 determinant (4 cases), and inducer/helper (OKT4) or cytotoxic/suppressor (OKT8) determinants (4 cases). Cells from two cases formed sheep RBC rosettes. The malignant cells all originated from B lymphocytes of the follicular center. The mechanism of development of cells with dual characteristics is uncertain, but may involve derepression of genetic material, transformation of a stem cell before divergence of B and T lymphocyte differentiation, or neoplastic expansion of a normal cell population that has dual markers. (25 Refs)

## 11. IMMUNOLOGIC, CLINICOPATHOLOGIC AND PROGNOSTIC FEATURES OF LYMPHOMA OF THE GASTROINTESTINAL TRACT.

Minato K, Shimoyama M, Saito H, Watanabe S
Sect. Hematology, Natl. Cancer Center Hosp., 1-1, Tsukiji 5-chome, Chuo-ku, Tokyo 104, Japan
Jpn J Clin Oncol; 11(2):353-362 1981

Surface marker characteristics of lymphoma cells from 32 patients with histopathologically proven malignant lymphomas with gastrointestinal tract (GI) involvement were investigated. Of 12 patients with primary lymphoma of the GI tract, 6 patients presented with masses in the stomach, 1 patient with a mass of the duodenum, 3 with masses in the ileocecal region, and 2 with multiple tumors of t he GI tract. In only 1/12 cases were tumor cells found to have no surface Ig (SIg), and to have E-rosette-forming capacity (ERFC) and human T-lymphocyte antigen (HTLA). Of the 11 other non-T lymphomas, 7 were positive for SIg, 2 were negative, and 2 were undetermined. In the seven B-cell lymphomas, SIg were mu heavy chain in four and gamma chain in three. All non-T lymphoma cells had Ia-like antigen. Of the 20 patients with secondary lymphoma of the GI tract, 6 patients had masses only in the stomach, 1 had masses in the small intestine, and two only in the ileocecal region. In 3/20 cases, tumor cells had no SIg, but had ERFC and/or HTLA. No T-cell markers were found in the other 17 cases. Of these, SIg were detected in eight cases bu not in five cases. All the cases examined, including T-cell type cases, showed Ia-like antigen. (22 Refs)

## 12. CONCENTRATION OF ROSETTE-FORMING CELLS AND FUNCTIONAL ACTIVITY OF PERIPHERAL BLOOD T-LYMPHOCYTES IN DIFFERENT STAGES OF HODGKIN'S DISEASE.

Loseva MI, Fridiland DIu
Dept. Therapy, Faculty Pediatrics, Medical Inst., Novosibirsk, USSR
Ter Arkh; 53(9):68-71 1981

Functional activity of peripheral blood lymphocytes was studied in 75 Hodgkin's disease patients (56% men, 44% women; median age group, 20-29 yr). Among these patients, 28 had Stage II disease, 28 had Stage III, and 19 had Stage IV. Prior to polychemotherapy, concentrations of T-rosette-forming cells in the Stage II, III, and IV patients were 29.6%, 24.1%, and 19.3%, respectively; macrophage migration indices were 54.9%, 61.3%, and 69.0%, respectively. The contents of B lymphocytes showed progressive increases from 20.1% for Stage II disease to 28.7% for Stage III and 29.5% for Stage IV. Polychemotherapy resulted in certain normalization of the immunological indices; however, during remission, the patients developed secondary imbalance of the content of immunocompetent cells. (8 Refs) (In RUS)

## 13. COMPARISON OF HISTOLOGIC AND IMMUNOLOGIC HETEROGENEITY OF NON-HODGKIN'S LYMPHOMAS.

Borowitz MJ, Croker BP, Metzgar RS
Dept. Pathology, Duke Univ. Medical Center, Box 3712, Durham, NC, 27710
Am J Pathol; 105(2):97-106 1981

The lymphocyte surface marker phenotype in 11 selected cases of non-Hodgkin's lymphomas was determined with anti-Ig and mouse monoclonal antibodies against human lymphocyte antigens. A complement-mediated cell cytotoxicity assay on suspensions of the tumor cells was compared with an indirect immunoperoxidase technique on frozen tissue sections. Both methods gave good results in tumors with a uniform cell population, but the frozen section technique was superior in heterogeneous tumors. The six B-cell neoplasms were heterogeneous with respect to expression of surface Ig and Ia antigens. The five T-cell tumors were morphologically heterogeneous and also highly variable in their expression of different T-cell s pecific antigens. (Author abstract) (33 Refs)

## 14. PURINE NUCLEOSIDE PHOSPHORYLASE (PNP) AND ADENOSINE DEAMINASE (ADA) ACTIVITIES EXAMINED CYTOCHEMICALLY IN UNFIXED LYMPHOCYTES OF PATIENTS WITH LYMPHOPROLIFERATIVE DISORDERS.

Maeda K, Ito K, Yamaguchi N
(c/o Ito) Blood Transfusion Service, Kobe Univ. Hosp., 7-5-2 Kusunoki-cho, Chuo-ku, Kobe 650, Japan
Blood; 58(5):897-903 1981

New techniques have been devised for the cytochemical demonstration of purine nucleoside phosphorylase (PNP) and adenosine deaminase (ADA) activities in unfixed human lymphocytes. A suspension of living lymphocytes is mixed with agarose soln containing the reagents for the detection of PNP or ADA activity on a glass slide. The mixture solidifies, is incubated, and then dried for light-microscopic observation. Reactive cells are recognized by the diffusely deposited granules of formazan, the end-product of the cytochemical reaction, and are divided into three groups of the cell with the low, middle, and high enzyme activity by the number of the granules. In healthy adults, the mean percentages of PNP- and ADA-positive cells were more than 90% in unfractionated lymphocytes, T-cell fractions, and complement-receptor cell fractions and cells with middle PNP and ADA activities were predominant. The PNP and ADA staining was observed in lymphoid cells of patients with lymphoproliferative disorders. A decrease in the percentage of PNP-positive cells concomitant with a relative increase of cells with the low enzyme activity was observed in the lymphocytes of nine patients with chronic lymphocytic leukemia (CLL). Similar findings were obtained in the ADA

staining of the lymphocytes of five patients with B-cell CLL. (Author abstract) (31 Refs)

### 15. THYMIDINE KINASE ISOENZYMES IN CHRONIC LYMPHOCYTIC LEUKAEMIA.

Ellims PH, Gan TE, Van der Weyden MB
Monash Univ. Dept. Medicine, Alfred Hosp., Commercial Road, Prahran 3181, Victoria, Australia
Br J Haematol; 49(3):479-481 1981

The profile of thymidine kinase isoenzymes were determined in peripheral blood lymphocytes from 14 patients with chronic lymphocytic leukemia (CLL) and 31 controls. Twelve patients with indolent disease showed TK2 isoenzyme activity, while two patients in whom the disease evolved and two patients who presented with aggressive disease exhibited TK1 isoenzyme activity. The demonstration of TK1 activity in the peripheral blood lymphocytes of clinically aggressive CLL suggests that this isoenzyme may be a useful biochemical marker of such behavior. (Author abstract) (6 Refs)

### 16. SURFACE MEMBRANE CHARACTERISTICS AND CYTOCHEMISTRY OF THE ABNORMAL CELLS IN NONLYMPHOCYTIC LEUKEMIA.

Ikeda S
Dept. Hematology, Atomic Disease Inst., Nagasaki Univ., Sch. Medicine, Sakamoto-cho, Nagasaki 852, Japan
Nippon Naika Gakkai Zasshi; 70(4):553-564 1981

The surface membrane characteristics and cytochemistry of the leukemia cells were determined in 20 patients with acute myelogenous leukemia (AML), 2 with acute premyelogenous leukemia (APL), 3 with chronic myelogenous leukemia with malignant change (CMLC), 2 with acute monocytic leukemia (AMoL), 12 with acute-subacute myelogenous monocytic leukemia (MMoL) and with chronic myelogenous monocytic leukemia (CMMoL). The cells were examined for Fcgamma, Fcmu, C3b and C3d receptors by the percentage of rosette-forming cells by means of a microtest plate. Human group AB serum and AKR mouse serum were used as complement. Phagocytosis of the leukemia cells was also determined. Since most of the patients having cytoplasmic granules and peroxidase (PO) among the patients with AML and APL had Fcgamma or C3 receptors, the receptors, granules and PO were considered to appear simultaneously. CML (with malignant change) patients had receptors although only a small amount of enzymes was expressed. All of the patients with AMoL and MMoL had several receptors, and phagocytosis was also detected in all of the patients. Cytochemically, 5 of the 18 patients with AMoL, MMoL or CMMoL completely lacked alpha-naphthyl butyrate esterase in their monocytic leukemia cells, and 7 of the patients partially lacked this enzyme. Phagocytosis was detected in all of the patients, even those who lacked this enzyme. Therefore, the finding of immunological phagocytosis was considered valuable as evidence that a monocytic element constituted the leukemia cell. (20 Refs) (In JPN)

### 17. T-CELL SUBPOPULATIONS IN MULTIPLE MYELOMA: CORRELATION WITH CLINICAL DISEASE STATUS.

Oken MM, Kay NE
Hematology Section (111E), Veterans Admin. Medical Center, 54th St. and 48th Ave. S., Minneapolis, MN, 55417
Br J Haematol; 49(4):629-634 1981

T-lymphocyte subpopulations bearing Fc receptors for IgM (Tmu) or for IgG (Tgamma) were studied in blood specimens obtained from 40 normal volunteers and from 16 patients with multiple myeloma. The myeloma patients showed a significant imbalance in T-cell subpopulations characterized by an increase in the percentages of Tgamma cells to 30.0 +-3.9% (mean +- SEM) compared with 12.0 +-3.0% for the controls (p less than 0.001). The patients exhibited a decreased proportion of Tmu cells (13.4 +-4.1%) compared with the control value of 55 +-7% (p less than 0.001). When the results were analyzed according to clinical status it was the patients with indolent or well-controled disease and not those with progressive disease who exhibited an elevated proportion of Tgamma cells. The elevation of Tgamma cells or of a subpopulation of suppressor cells should be further studied as a possible mechanism of disease control in multiple myeloma. (Author abstract) (19 Refs)

### 18. ACUTE LEUKAEMIA, PERSPECTIVES IN DIAGNOSIS AND TREATMENT.

Zwaan FE, Jansen J
Dept. Internal Medicine, Univ. Hosp., Rijnsburgerweg 10, 2333 AA Leiden, Netherlands
Neth J Med; 24(5):190-194 1981

Perspectives in diagnosis and treatment of acute leukemia are reviewed. Advances in cytochemical, immunologic, cytogenetic, and in vitro culture methods allow most centers to identify the neoplastic cell involved in any individual case. One method is the FAB classification for acute non-lymphocytic leukemia (ANLL), based on morphologic features and cytochemical reactions. Antigens detectable by immunofluorescence methods are useful for distinguishing subtypes of acute lymphocytic leukemia (ALL). Presence of the 'common ALL' antigen is correlated with good prognosis, whereas markers for T- and B-cells (sheep RBC receptors) usually indicate poor prognosis. New markers holding promise for differentiation of ALL subtypes include terminal deoxynucleotidyl transferase and the Ia-like antigens. Techniques for culturing normal progenitor cells have aided in the prediction of leukemic relapse; recent development of techniques for culturing leukemic progenitor cells may aid in selecting cytotoxic chemotherapeutic agents. Discovery of the Philadelphia chromosome and other translocations may be useful in cytogenetic diagnosis and determination of prognosis. Excellent results in the treatment of childhood ALL have been achieved with protocols based on 'total therapy,' which include remission induction chemotherapy, CNS prophylaxis with cerebral irradiation, and maintenance chemotherapy. ANLL has a poor prognosis, but modified supportive care has improved therapeutic results. Allogeneic bone marrow transplantation has been of limited success in acute myeloid leukemia. New techniques for prevention or suppression of immunologic interaction between donor and recipient must be evaluated. (26 Refs)

### 19. BIOLOGICAL AND IMMUNOLOGICAL MARKERS IN ACUTE LEUKAEMIA.

Lopez Borrasca A, Gonzalez M, Hernandez F, Ledesma M, Corrales A, San Miguel J
Servicio de Hematologia, Hospital Clinico Universitario, Salamanca, Spain
Sangre (Barc); 26(5B):756-782 1981

The authors present a review of the value of immunologic and enzymatic markers in the diagnosis of the different types of acute leukemia (AL). The addition of such markers to the classical morphologic and cytochemical criteria is advisable since they provide the means for AL subclassifications to be used with therapeutical purposes. The markers are divided into

(a) surface receptors: sIg, C receptors, Fc receptors, non-immunologic spontaneous rosettes with different red-cells and viral receptors; and (b) surface antigens, including T-lymphocytes surface antigen, B-lymphocyte antigens, common ALL antigen and myeloid cells antigen. Their significance is detailed, along with other data including their study tech niques, the levels in different leukemic populations, and the value of such markers in the immunologic differential-diagnosis of the leukemias. The enzymatic markers, terminal deoxynucleotidyl transferase, adenosine-deaminase, nucleoside-phosphorylase, 5'-nucleotidase, and hexosaminidase (N-acetyl-B-glucosaminidase) are considered. Following the pattern referred to, an analysis is made of the significance of, and study methods for, these sort of markers, along with their clinical interest and the correlation they may show with the immunologic markers mentioned above. Classifications are suggested based on the phenotypes of the leukemic cells. These phenotypes correspond to T-cell, B-cell, and non-T, non-B lymphoblastic leukemias, as well as to the blastic crises of chronic granulocytic leukemia; and the phenotypes of the acute myeloblastic leukemias are also considered. The application of the methodology commented in this paper has provided a new variant, the pre-B acute leukemia, which is characterized by possessing cIgM. (173 Refs) (In SPA)

## DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS

### 20. SIMULTANEOUS ANALYSIS OF DNA AND CELL SURFACE IMMUNOGLOBULIN IN HUMAN B-CELL LYMPHOMAS BY FLOW CYTOMETRY.

**Kruth HS, Braylan RC, Benson NA, Nourse VA**
**(c/o Braylan) Dept. Pathology, Univ. Florida Coll. Medicine, Gainesville, FL, 32610**
**Cancer Res; 41(12):4895-4899 1981**

Cell suspensions prepared from human B-cell lymphomas were analyzed for cellular DNA and cell surface Ig (SIg) by flow cytometry. In addition to SIg-bearing neoplastic B-lymphocytes, these tumors contain nonneoplastic cells. Flow cytometry permitted selective analysis of DNA in subpopulations defined by the membrane antigen SIg and also permitted analysis of SIg of subpopulations defined by DNA content. Because measurements of DNA and SIg were made simultaneously on each cell, physical separation of cells was not required. Using propidium iodide as a fluorescent DNA probe and fluorescein isothiocyanate-labeled antibodies to stain SIg, differences in cellular DNA between SIg-bearing neoplastic cells and nonneoplastic cells from the same tissues could be demonstrated. Additionally, this simultaneous correlated analysis allowed assessment of the cell cycle dependence of SIg expression. Mean fluorescein isothiocyanate (SIg) fluorescence was greater in S- than G1-phase cells, but the ratio of mean fluorescein isothiocyanate fluorescence of cells in S phase to that of cells in G1 phase varied for different tumors. (Author abstract) (22 Refs)

### 21. T CELL GROWTH FACTOR RECEPTORS. QUANTITATION, SPECIFICITY, AND BIOLOGICAL RELEVANCE.

**Robb RJ, Munck A, Smith KA**
**Immunology Program, Norris Cotton Cancer Center, Hanover, NH, 03755**
**J Exp Med; 154(5):1455-1474 1981**

T cell growth factor (TCGF) interactions were studied in several cell lines. TCG F bound specifically to receptor sites on activated T cells, producing proliferative response. Unstimulated murine or human lymphocytes and lipopolysaccharide-activated B cell blasts expressed few if any detectable binding sites. Lectin- or alloantigen-activated cells had easily detectable receptors. TCGF-independent T cells did not bind TCGF. (45 Refs)

### 22. POPULATIONS OF KILLER CELLS AND T-CELLS BEARING RECEPTORS FOR IGG IN LYMPHOPROLIFERATIVE DISORDERS, WITH SPECIAL REFERENCE TO ADULT T-CELL MALIGNANT LYMPHOMA-LEUKEMIA.

**Yagi Y, Hasui K, Sato E**
**Second Dept. Pathology, Kagoshima Univ., 1208-1, Usuki-cho, Kagoshima 890, Japan**
**Jpn J Clin Oncol; 11(2):299-306 1981**

Killer T-cells (K) which act as effector cells of antibody-dependent cell-mediated cytotoxicity (ADCC) and of T cells bearing receptors for the Fc portion of IgG (TG) were studied in preparations obtained from patients with peripheral T-cell malignant lymphoma-leukemia (PTML) and other lymphoproliferative disorders. Of the 43 patients studied, 26 had PTML, 5 had mycosis fungoides, 6 had B-cell malignant lymphoma, 1 had null cell malignant lymphoma, 2 had plasma cell dyscrasia, and 3 had multiple myeloma. Fewer K-cells were found in the peripheral blood of patients with lymphoproliferative disorders, while TG cells varied widely in number. Leukemia patients showed significantly fewer K cells than non-leukemia patients. Significant increases in TG cells were observed in some PTML patients. Leukemic cells of patients with adult T-cell leukemia and the tumor cells of lymph nodes had no ADCC activity. (35 Refs)

### 23. STUDIES ON T CELL BEARING FC RECEPTORS FOR IGG OF PERIPHERAL LYMPHOCYTES IN PATIENTS WITH BLADDER CARCINOMA.

**Shimatani N**
**Dept. Urology, Kobe Univ. Sch. Medicine, Kobe, Japan**
**Hinyokika Kiyo; 27(6):637-647 1981**

To test the cellular immunocompetence in patients with bladder carcinoma, a study was made on the lymphocyte subpopulation of 34 patients and 35 healthy men. T cell was identified by spontaneous rosette formation with sheep RBC, and B cell was identified by EAC rosette formation. T lymphocytes bearing Fc receptors for IgG (IgGFcR+ T cells) were detected by double rosette formation of neuraminidase treated sheep RBC and glutaraldehyde treated sensitized ox RBC. The percentages of IgGFcR+ T cells in total T cells in peripheral lymphocytes of 35 healthy men and 34 untreated bladder cancer patients were 5.8 +-1.9% and 14.2 +-8.4% respectively, the percentages of T cells in peripheral lymphocytes of 35 healthy men and 34 untreated bladder cancer patients were 81.3 +-6.3% and 68.6 +-14.0% respectively. The difference between these figures was statistically significant. There was a

tendency to decrease in percentage and absolute count of T cells in the patients with higher grade and stage of the tumor. Contrary, there was a ten dency to increase percentages of IgGFcR+ T cells in total T cells of the patients with higher grade and stage of the tumor. No influence of operation was found on T cell percentage, absolute count of T cell and the percentage of IgGFcR+ T cells in total T cells. Steroids which were secreted by stimulation of operative stress might have an effect on the percentages of IgGFcR+ T cells in total T cells. (Author abstract) (33 Refs) (In JPN)

### 24. HUMAN AUTOLOGOUS ROSETTES. II. FURTHER CHARACTERIZATION: MARKERS AND FUNCTIONS.

**Rucheton M, Caraux J, Rey A, Thierry C, Esteve C, Valles H, Dufer J, Desplaces A, Zagury D, Serrou B**
**Laboratoire d'Immunopharmacologie des Tumeurs, INSERM U 236, ERA-CNRS No., ERA-CNRS No 844, Centre Paul Lamarque, Hopital St. Eloi, B.P. 5054, 34033 Montepellier Cedex, France**
**Cell Immunol; 64(2):312-323 1981**

Purification of peripheral blood lymphocytes able to form autologous rosettes (ARFC) overnight has been obtained with satisfactory yield and enrichment, using short-term centrifugation on a Percoll cushion. Purified ARFC form E-rosettes, express human T-lymphocyte antigens, and contain cell-bearing Fc receptors for IgM but very few for IgG. They are also OKT4 positive. Morphological structure and cytochemistry (beta-glucuronidase and acid phosphatase) do not suggest activation. The ARFC subset has poor antibody-dependent cell-mediated cytotoxicity and NK activity. They respond strongly to PHA and demonstrate a higher response in mixed allogeneic or autologous culture compared to non-ARFC or total PBL. (Author abstract) (42 Refs)

### 25. SERUM FACTORS INHIBITING E-ROSETTE FORMATION IN PATIENTS WITH LUNG MALIGNANCIES.

**Saiz-Garcia F, Rodriguez-Valverde V**
**(c/o Rodriguex-Valverde) Seccion de Reumatologia, Centro Medico Nacional 'Marques de Valdecilla', Santander, Spain**
**Bull Cancer (Paris); 68(4):346-349 1981**

Data supporting the existence of serum factors able to inhibit the formation of RBC (E)-rosettes by peripheral blood lymphocytes (PBL) of 13 patients (mean age 62.5 yr) with lung cancer (3 squamous cell, 2 anaplastic large cell, 3 anaplastic small-cell, 2 alveolar-carcinoma, 1 adenocarcinoma, and 2 unknown) are presented. Seven normal individuals (mean age 47.5 yr) were used as controls. The 13 cancer patients had a low baseline proportion of E-rosetting cells: 40.12 +-6.6% as compared to a normal value of 58.87 +-5.53% (p less than 0.0005). After overnight incubation in medium with 20% fetal calf serum (FCS) or normal pooled AB serum, the proportion of PBL able to form E-rosettes increased to normal levels in 13/13 patients. No such increase was observed in controls. When PBL from cancer patients which had regained the ability to form E-rosettes by incubation with FCS were further incubated with medium containing 20% of heat-inactivated autologous serum, the proportion of E-rosettes dropped to preincubation values. No significant influence on the number of E-rosette forming cells was observed when the sera from cancer patients were used in cultures with normal lymphocytes or with lymphocytes from a different lung cancer patient. In only one case was there a drop in the number of E-rosette forming cells. In this case, both lymphocytes and serum were from patients with cancer of the same histological type. E-rosette deficiency in patients with lung cancer is discussed. (15 Refs)

### 26. INHIBITION OF LEUKOCYTE MIGRATION IN WOMEN WITH OVARIAN CARCINOMA AND ITS DEPENDENCE ON THE QUANTITY OF LYMPHOCYTES FORMING E-ROSETTES.

**Tosner J, Vejbora O, Fixa B**
**Gynekologicko-porodnicka klinika, Fakultna nemocnica s poliklinikou KUNZ VcKNV, Engelsova 374, 500 06 Hradec Kralove, Czechoslovakia**
**Cas Lek Cesk; 120(38):1150-1154 1981**

Leukocyte migration inhibition (LMI) and the number of E-rosette forming lymphocytes and their possible correlation were studied in 20 women with ovarian carcinoma. Mucinous cystadenopapillary carcinoma was diagnosed in 2 cases, solid undifferentiated carcinoma in 6, and serous cystadenopapillary carcinoma in 12. The migration index (MI) for the entire group was 74.76, and the av percentage of E-rosettes was 40.46%. The MI was 61.8 in patients who had been in remission for at least 3 mo, 80.6 in the patients with progression of the disease ($p = 0.05$), and 85.6 in tumor-free controls. The percentages of E-rosettes were 40.46% in the entire group; 34.61% in the patients with progressive tumor growth, 41.35% in the patients in remission, and 44.0% in the controls, which latter was significantly higher than in the patients with progressive tumor growth. There was no significant correlation between the leukocyte migration inhibition and the percentage of E-rosette forming lymphocytes for the whole group (correlation factor 0.31), but the correlation factor was 0.55 for the patients with progressive tumor growth and 0.52 for those in remission, which suggests the existence of a correlation. (16 Refs) (In CZE)

## LYMPHOCYTE AND DIFFERENTIATION ANTIGENS

### 27. THE ROLE OF THE MAJOR HISTOCOMPATIBILITY COMPLEX IN IMMUNOBIOLOGY.

**Dorf ME**
**Harvard Medical Sch., Boston, MA**
**The Role of the Major Histocompatibility Complex in Immunobiology. New York, Garland STPM Press, 406 pp., 1981.**

Products of the major histocompatibility complex (MHC) and their functions, structure, and genetic conirol are discussed. The MHC is able to mount specific immune responses to distant thymus-dependent antigens, develop mixed WBC reactions in culture, regulate immune responses by controlling essential antigen-dependent cellular interactions of the immune system, develop specific suppressor T cells, and interact with the complement system. Topics discussed include the genetic fine structure of the mouse H-2 gene complex, antigens of the TLA region of the mouse genome, genetics and biology of the human leukocyte antigen system, biochemical analysis of MHC products, complement and the MHC, genetic control of immune responsiveness, cellular interactions, role of the MHC in delayed type hypersensitivity, specific T cell factors with MHC determinants, specificity of cytolytic T cell responses, and tumor immunity and the MHC. (1478 Refs)

## 28. INDICATION OF B-LYMPHOCYTIC LEUKEMIA BY MONOCLONAL ANTIBODY ANTI-Y 29/55.

Obrecht JP, Gudat F, Forster HK, Albrecht R, Girard MF, Ludwig C, Christen C
Onkologie, Kantonsspital, Petersgraben, 4, CH-4031 Basel, Switzerland
Schweiz Med Wochenschr; 111(41):1529-1531 1981

The monoclonal antibody anti-Y 29/55 recognizes a group specific antigen on sessile human B-lymphocytes which do not belong to the recirculating lymphocyte pool. The occurrence of this antigen in malignant NHL, with or without leukemic state, and in other leukemias has been studied. The antigen was expressed on cells of various histologic B-cell types but not on leukemic cells of ALL, T-lymphoma, AML or CML. It is concluded that in malignant B-lymphoma, B-CLL and HCL, cells appearing in blood carry a marker characteristic of virgin or activated sessile B-lymphocytes. Anti-Y 29/55 permits differentiation of such cells from normal recirculating B-cells and other leukemic cells including ALL, AML and CML. In follow-up studies this antibody may be helpful in detecting early leukemia output. B-lymphocytic leukemia may reflect a disproportion between binding sites on the lymphatic reticulum and the neoplastic cells bearing this antigen, which might be involved in binding of B-lymphocytes to the supporting lymphatic reticulum. (Author abstract) (3 Refs) (In GER)

## 29. MONOCLONAL ANTIBODIES RECOGNIZING NORMAL HUMAN T LYMPHOCYTES AND MALIGNANT HUMAN B LYMPHOCYTES: A COMPARATIVE STUDY.

Martin PJ, Hansen JA, Siadak AW, Nowinski RC
Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104
J Immunol; 127(5):1920-1923 1981

We have undertaken a direct comparison of eight different murine monoclonal antibodies that recognize antigens shared by human T cells and certain malignant B cells. Immune precipitation, lysostripping, and competitive binding experiments indicate that the antigenic determinants detected by antibodies Leu 1, T101, 17F12, SC1, A50, OKT1, and 10.2 are closely associated on the same molecular species and may in fact be identical. The antigenic determinant recognized by antibody 12.1, which has properties similar to the one detected by other antibodies, is present on a distinct cell-surface molecule. Our results emphasize the importance of a quantitative direct comparison of different monoclonal antibodie s in distinguishing newly reported antibodies from those already described. Such a comparison can resolve apparent discrepancies that arise either from methodologic variations or from differences in antibody avidity. (Author abstract) (21 Refs)

## 30. T LYMPHOCYTE SUBSETS IN PATIENTS WITH MALIGNANT MELANOMA.

Karavodin LM, Giuliano AE, Golub SH
Div Oncology, Dept. Surgery, UCLA Sch. Medicine, Los Angeles, CA, 90024
Cancer Immunol Immunother; 11(4):251-254 1981

The value of T lymphocyte subset profiles as an indicator of disease progression in malignant melanoma (MM) was studied. Cryopreserved lymphocytes from 57 MM patients and 19 normal individuals were assayed. Monoclonal antibodies were used to identify lymphocyte populations: OKT3.PAN for total peripheral T cells, OKT4.IND for inducer-helper subclass, and OKT8.SUP for suppressor-cytotoxic subclass. Analysis of subset profiles indicated no correlation between any of the subset values and presence or absence of disease, stage of disease, clinical outcome, age, or sex of the patients. A sequential study of three patients with recurrent disease showed no predictable variation of values during the course of the disease. Results indicate no systemic imbalance among T cell subsets in MM. More localized T cell imbalance, such as in lymph nodes adjacent to the tumor, is suggested as a possibility. (19 Refs)

## 31. MOLECULAR COMPLEXITY OF LEUKOCYTE SURFACE GLYCOPROTEINS RELATED TO THE MACROPHAGE DIFFERENTIATION ANTIGEN MAC-1.

Trowbridge IS, Omary MB
Dept. Cancer Biology, Salk Inst. for Biological Studies, San Diego, CA, 92138
J Exp Med; 154(5):1517-1524 1981

A differentiation antigen designated Mac-1 was identified on murine macrophages using the monoclonal antibody M1/70. Mac-1 belongs to a family of structurally and antigenically related glycoproteins found on a variety of hemopoietic cells including phagocytes and other cell types. The functional significance of these glycoproteins is discussed. (24 Refs)

## 32. LY-18, A NEW ALLOANTIGEN PRESENT ON CYTOTOXIC T CELLS AND CONTROLLED BY A GENE(S) LINKED TO THE IGH-V LOCUS.

Finnegan A, Owen FL
(c/o Owen) Cancer Res. Center, Tufts Univ. Med. Sch., 136 Harrison Ave., Boston, MA, 02111
J Immunol; 127(5):1947-1953 1981

Antiserum raised in allotype-congenic mice recognizes a T cell differentiation antigen designated Ly-18. This antiserum was raised by immunization of (CB.20 x CBA-Igh-1b)F1 mice with secondary BALB/c anti-CBA allospecific cytotoxic cells. This antigenic specificity is expressed on cytotoxic T cells but not on cells proliferating in an MLR, plaque-forming cells specific for SRBC, or resting lymphoid cells. The expression of Ly-18 is controlled by gene(s) linked to the VH gene complex of Igh-1 allotype strains. There is no evidence at present for MHC gene control. Unlike other putative antibodies against antigen receptors, anti-Ly 18 does not block cytotoxicity. In addition, Ly-18 expression is not altered by the antigenic specificity of the Igh-1 effector. We conclude Ly-18 is a differentiation antigen present on a subpopulation of activated T cells. The gene(s) that codes for expression of Ly-18 is linked to the expression of Igh-1 genes. (Author abstract) (39 Refs)

## 33. A NEW MOUSE CELL-SURFACE ANTIGEN (LY-M20) CONTROLLED BY A GENE LINKED TO MLS LOCUS AND DEFINED BY MONOCLONAL ANTIBODIES.

Kimura S, Tada N, Nakayama E, Liu Y, Hammerling U
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Immunogenetics; 14(1/2):3-14 1981

Five monoclonal antibodies were established by the fusion of mouse myeloma cells (NS.1) with spleen cells from A and (A x C3H/An)F1 mice hyperimmunized with 70Z/3 tumor cells. These antibodies recognized a new antigenic specificity provisionally called Ly-m20.2. In direct cytotoxicity assays, 60% of cells in spleen, 40% in lymph node, 50% in bone marrow and less than 5% in thymus were found to react with three of the five antibodies, whereas the two others yielded somewhat lower cytotoxicity indices. The Ly-m20.2 antigen was also expressed on cells derived from liver and kidney but not on cells derived from brain. As judged from cytotoxicity assays with separated T and B cells, Ly-m20.2 antigen is carried preferen-

tially on B lymphocytes. Direct plaque-forming cells were completely eliminated by Ly-m20.2-specific antibody and complement. Linkage tests by analysis in 20 (CBA/J x C3H/An) x C3H/An backcross mice and by segregation analysis of BXH and SWXL recombinant inbred strains indicate close association of the loci controlling ly-m20.2 and Mls antigens on chromosome 1. (Author abstract) (30 Refs)

### 34. STUDIES ON NATURAL KILLER (NK) CELLS. II. SEROLOGIC EVIDENCE FOR HETEROGENEITY OF MURINE NK CELLS.

Burton RC, Bartlett SP, Kumar V, Winn HJ
Transplantation Unit, General Surgical Services, Harvard Medical Sch. Massachusetts General Hosp., Boston, MA, 02114
J Immunol; 127(5):1864-1868 1981

NK cells are divided into two subclasses on the basis of cell surface antigens: NKA cells, which preferentially lyse lymphoma cells and which are readily destroyed by treatment with anti-H-2, rabbit anti-mouse, or anti-NK specific antibodies in the presence of C; and NKB cells, which preferentially lyse nonlymphoma tumor cells and which are resistant to anti-NK specific antibodies, partially sensitive to anti-H-2 specific antibodies, and only fully sensitive to rabbit anti-mouse serum and C. Thus, suspensions of spleen cells that were treated with anti-NK-1.2 antibodies and C lost virtually all lytic activity for six lymphoma cell lines, whereas lytic activity for two nonlymphoma cell lines remai ned largely intact. It must be noted, however, that unlike NK-1.2 expression, target cell preference is not an absolute indicator of NK cell subclass. Cytotoxic T cells were readily distinguished from NKA and NKB cells on the basis of their sensitivity to monoclonal anti-Thy1.2 antibodies and resistance to anti-NK-1.2 antiserum and C. (Author abstract) (23 Refs)

## CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION

### 35. EXPRESSION OF RECEPTORS FOR IGA IN HAIRY-CELL AND OTHER B-CELL LEUKAEMIAS.

Lydyard PM, Powell RG, Fanger MW, Worman CP, Cawley JC
Dept. Immunology, Middlesex Hosp. Medical Sch., Arthur Stanley House, 40-50 Tottenham St., London W1P 9PG, England
Br J Haematol; 49(4):643-647 1981

In six cases of both hairy-cell leukemia (HCL) and chronic lymphocytic leukemia (CLL) it was shown that the pathological cells express receptors for the Fc portion of IgA (RFcalpha). Many of the cells simultaneously expressed receptors for IgA, IgM and IgG, and blocking studies showed that these are distinct receptors. In contrast, the malignant cells of most of the various other B-cell leukemias studied showed low levels of RFcalpha expression. The significance of the results is briefly discussed and it is suggested that receptor expression may be a marker of certain stages of B-cell development. (Author abstract) (14 Refs)

### 36. COMPARISON OF MONOCYTE AND ALVEOLAR MACROPHAGE ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY AND FC-RECEPTOR ACTIVITY.

Garagiola DM, Huard TK, LoBuglio AF
Simpson Memorial Inst., Univ. Michigan, Ann Arbor, MI, 48109
Cell Immunol; 64(2):359-370 1981

The cytotoxic potential of rabbit peripheral blood monocytes and alveolar macrophages in antibody-dependent cellular cytotoxicity (ADCC) toward both RBC (RBCox) and tumor cell (CEM T-lymphoblast) targets was examined. ADCC was measured in a 4-hr 51Cr-release assay. Alveolar macrophages were more efficient at killing the tumor cell targets (optimally sensitized with rabbit antisera) than monocytes at similar effector cell/target cell (E/T) ratios. Tumor cell targets sensitized with with seven different antisera (anti-CEM) were lysed by alveolar macrophages but not by the monocytes. In marked contrast the monocytes were more effective at lysing the sensitized RBC target cells. The degree of cytolysis of RBCox and CEM was dependent on the E/T ratio and the degree of sensitization of these target cells. It was demonstrated that the effector cell selectivity in ADCC was directly related to their ability or inability to bind the sensitized target cells as determined by Fc-receptor rosette formation. The transition from monocyte to macrophage may, therefore, have resulted in an alteration in the criteria necessary for Fc-receptor binding to antibody-sensitized target cells and subsequent ADCC. (Author abstract) (40 Refs)

### 37. ADENOSINE 5'-TRIPHOSPHATE- (ATP) MEDIATED STIMULATION AND SUPPRESSION OF DNA SYNTHESIS IN LYMPHOID CELLS. I. CHARACTERIZATION OF ATP RESPONSIVE CELLS IN MOUSE LYMPHOID ORGANS.

Ikehara S, Pahwa RN, Lunzer DG, Good RA, Modak MJ
(c/o Pahwa), Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
J Immunol; 127(5):1834-1838 1981

The effects of various nucleotides and nucleosides on DNA synthesis of mouse lymphocyte populations were studied. Significant stimulation of DNA synthesis was observed in the cells from bone marrow or the thymus in the presence of ATP. In contrast, the DNA synthesis of the cells from spleen, lymph nodes, and peripheral blood was markedly inhibited by ATP. Guanosine 5'-triphosphate had nonspecific stimulatory effects on the DNA synthesis of various lymphoid cells, whereas cytidine triphosphate had no effect. When the thymocytes or bone marrow cells were separated by 1 x g velocity sedimentation, a distinct cell population was identified as being responsible for the ATP-mediated stimulation of DNA synthesis. Further characterization of ATP-responsive cells revealed that the highest concentration of terminal deoxynucleotidyl transferase, a marker enzyme for precursor T cells, was present in these cells. ATP-mediated stimulation of DNA synthesis may, therefore, serve as a specific marker restricted to a certain population of differentiating T cells. (Author abstract) (32 Refs)

## 38. HETEROGENEITY IN SURFACE GLYCOPROTEINS OF MOUSE PERITONEAL MACROPHAGE POPULATIONS.

Kapian G, Olstad R
Inst. Medical Biology, Univ. Tromso, Tromso, Norway
Exp Cell Res; 135(2):379-386 1981

Murine peritoneal macrophages were activated in vitro by repeated addition to the culture medium of cell-free tumor ascites fluid from a syngeneic methylcholanthrene-induced sarcoma. Cell morphology was studied by phase-contrast microscopy and scanning electron microscopy (SEM). The ascites-activated cells were extensively spread out on the glass surface and showed extensive membrane ruffling. To investigate the protein metabolism of the cells, total protein content and incorporation and turnover of [14C]glucosamine and [35S]methionine into TCA-precipitable macromolecules were analyzed. Activated cells had a total protein content 2-3x higher than that found in control cells. [35S]Methionine and [14C]glucosamine were incorporated into ascites-treated cells at a rate 2.7-3x higher than into control cells. Cell glycoproteins were lost with biphasic kinetics with a reduced half-life for both phases in the activated cells as compared to controls. Radiolabelled proteins were isolated from the plasma membrane by immunoprecipitation of trinitrobenzene sulfonic acid-derived cells and analyzed by sodium dodecyl sulfate (SDS) polyacr ylamide gel electrophoresis. Whereas most of the protein peaks were the same in both cultures, the control cells had a single broad protein peak in the range of 100-110 K, whereas the ascites-activated cells had three peaks of 90, 100-110 and 135 K. The 135 K peak appeared to be a 'new' surface glycoprotein expressed in the activated but not in the control cells. (Author abstract) (29 Refs)

## 39. LOSS OF RECEPTOR ACTIVITY FOR MOUSE ERYTHROCYTES PRECEDES TUMOUR PROMOTER-INDUCED MATURATION OF CHRONIC LYMPHOCYTIC LEUKEMIA CELLS.

Forbes IJ, Zalewski PD, Valente L, Murray AW
Dept. Medicine, Queen Elizabeth Hosp., Woodville, Australia
Cancer Lett; 14(2):187-192 1981

Induction by 12-O-tetradecanoylphorbol-13-acetate (TPA) of chronic lymphocytic leukemia (CLL) cell differentiation and rapid, irreversible loss of mouse RBC (M) rosetting by leukemic B lymphocytes is reported. Lymphocytes from two patients with BM+ type CLL were cultured in the presence of 5 x 10(-7) M or 5 x 10(-9) M TPA. After 22 hr, the majority had a uropod, vacuoles, and markedly basophilic cytoplasm, with cytoplasmic immunoglobulin (CIg) of the same isotype as surface immunoglobulin (SIg). M rosetting capacity was completely inhibited. Mezerein was as effective as TPA in abolishing M rosetting and inducing CIg. Loss of the capacity of BM+ cells to rosette with mouse RBC was a very early effect of TPA seen in lymphocytes from six CLL patients. These experiments provide direct evidence that BM+ cells are precursors of BM- cells in human B cell differentiation. (12 Refs)

## 40. IMMUNE INTERFERON INDUCTION BY A MONOCLONAL ANTIBODY SPECIFIC FOR HUMAN T CELLS.

Pang RH, Yip YK, Vilcek J
(c/o Vilcek), New York Univ. Sch. Medicine, 550 First Ave., New York, NY, 10016
Cell Immunol; 64(2):304-311 1981

OKT3, a monoclonal antibody reactive with a surface antigen shared by all human T lymphocytes, was found to act as a potent interferon (IFN) inducer in cultures of human mononuclear WBC. Two other monoclonal antibodies reactive with T-cell subpopulations failed to induce IFN. IFN-inducing activity of OKT3 was similar to that of phytohemagglutinin (PHA). The phorbol ester, 12-O-tetradecanoylphorbol-13-acetate (TPA) had a strong potentiating effect on IFN production stimulated with OKT3 or PHA. IFN produced after stimulation with OKT3, like PHA-induced IFN, had properties characteristic for 'immune' IFN (IFN-gamma). (Author abstract) (26 Refs)

## 41. NORMAL AND NEOPLASTIC LYMPHOCYTE MATURATION.

Weissman IL, McGrath MS, Pillemer E, Hollander N, Rouse RV, Jerabek L, Stevens SK, Scollay RG, Butcher EC
Lab. Experimental Oncology, Stanford Univ. Sch. Medicine, Stanford, CA, 94305
J Supramol Struct Cell Biochem; 15(3):303-314 1981

Maturation of normal and neoplastic lymphocytes is described. Inducer lymphocyte s carry the marker Lyt 1 and recognize allogeneic cells or foreign antigens on the basis of the major histocompatibility complex (MHC) I. Cytotoxic T cells carry the markers Lyt 2 and 3 and recognize allogeneic cells or foreign antigens on the basis of K/D markers. Most T lymphocytes are small cells in G0 phase. G0 Lyt 1 cells recognize region I markers and produce T cell growth factor, which maintains proliferation of other T lymphocytes, including at least some Lyt2 and 3 cells. Thymocyte precursors originate from cells in the yolk sac and are produced throughout life in the bone marrow. Lymphoblasts are located mainly in the thymic cortex and produce T lymphocytes, some of which migrate to the thymic medulla or to other organs. In the thymus lymphocyte come in contact with nurse, cortical thymic epithelial, and spatulate epithelial cells, which bear K/D and I MHC markers. Migration and peripheral location of maturing T and B cells is controlled by surface receptors expressed on the cell surface. Lymphomagenesis may result from binding of retroviruses to lymphocytes bearing specific antigen-specific receptors for retrovirus envelope moieties. Infection of the lymphocytes by the virus would then result in production of viral envelope material, triggering increasing abnormal proliferation of lymphocytes. (50 Refs)

## 42. IMMUNITY IN PATIENTS WITH MALIGNANT OVARIAN NEOPLASMS.

Markowska J, Tomaszkiewicz T, Simm S, Jankowiak S
Klinika Onkologii, AM w Poznaniu, ul. Lakowa 1/2, 61-878 Poznan, Poland
Ginekol Pol; 52(8):729-737 1981

Correlations between the E rosette test and seven skin tests (pollen, phytohemagglutinin, purified protein derivative, streptokinase-streptodornase, Candida albicans, dinitrochlorobenzene, and Trychophyton rubrum) were performed in 57 patients with ovarian carcinoma. The E rosette test was performed with tumor-specific antigen in 26/57 patients. Correlation was found between the delayed skin hypersensitivity tests and the E rosette test performed with the tumor-specific antigen. The existence of the correlation suggests the necessity to differentiate the T lymphocytes to subpopulations participating in general and tumor immunity. Both tests give a better insight into the patient's immune status and may be useful in therapy planning. (13 Refs) (In POL)

### 43. INCREASED CIRCULATING TALPHALYMPHOCYTE POPULATION IN BRONCHOGENIC AND COLONIC CARCINOMA.

Pucci A, Clancy RL, Doe WF

Dept. Medicine, Royal North Shore Hosp., St. Leonards 2065, New South Wales, Australia

Clin Exp Immunol; 46(1):130-133 1981

The proportion of T lymphocytes bearing membrane receptors for IgA (Talpha cells) was markedly increased in the peripheral blood of patients suffering from cancers of the colon and bronchus compared to an age-matched normal population and to age-matched control patients being treated for non-mali gnant chronic inflammatory conditions of the intestine and lung. By contrast, the percentage of the T lymphocyte population having Fc-IgG receptors (Tgamma cells) and Fc-IgM receptors (Tmu cells) in mucosal malignancy was similar to that found in the two control populations. It is suggested that the increased percentage of Talpha cells found in colonic and bronchogenic carcinoma patients may reflect an as yet unknown regulatory function for this subset. (Author abstract) (7 Refs)

## EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS

### 44. PARTIAL NORMALIZATION OF B-CELL FUNCTION BY LEVAMISOLE IN ACUTE LYMPHOBLASTIC LEUKEMIA.

Diez RA, Estevez ME, Sen L

Inst. Investigacious Hematologicas, Academia Nacional de Medicina, Las Heras 3092, Buenos Aires 1425, Argentina

Medicina (B Aires); 41(4):471-475 1981

The functional capacity of B lymphocytes induced by pokeweed mitogen (PWM) to differentiate into plasma cells was investigated in acute lymphoblastic leukemia (ALL) patients in continuous complete remission (CCR) with and without levamisole. Mononuclear cells were obtained from 15-20 ml of blood from each of 14 ALL patient receiving levamisole along with cytotoxic drugs and 7 ALL patients receiving cytotoxic drugs only. Two million cells were treated with rabbit IgG antihuman total immunoglobin conjugated with fluorescein isothiocyanate and examined for surface immunoglobulin. Cells treated with PWM were incubated and examined for cytoplasmic immunoglobulin. Surface antigens were observed in 7.4% of normal patients and 5.4% of ALL patients. Cytoplasmic immunoglobulin in cells cultured with PWM were observed in 4.39% of normal patients, 2.34% of ALL patients receiving chemotherapy plus levamisole, and 0.17% in ALL patients receiving chemotherapy alone. Significantly lower differentiation ability was observed between normal patients and both groups of ALL patients. These results suggest that cytotoxic chemotherapy could induce an intrinsic defect in B cell ability to differentiate or interfere with plasma cell differentiation or regulation, and that levamisole is capable of partly correcting this defect. (18 Refs)

### 45. CONSIDERATIONS ABOUT THE USE OF LEVAMISOLE IN PATIENTS AFFECTED BY PRIMARY CANCER.

Marzo C, Gnasso P, Gennarelli E, Vitiello N, Borrelli G, Pasquinucci S, Antropoli L

Istituto di Clinica Tisiologica, I Facolta di Medicina e Chirurgia dell'Universita degli Studi di Napoli, Napoli, Italy

Rass Int Clin Ter; 61(5):289-293 1981

This study was undertaken to elucidate some aspects of levamisole (Le) effect on primary lung cancer. Advantageous and undesirable side effects were studied. All 51 patients with lung cancer diagnosis had tests in vivo for recall antigen (paraphenylenediamine - PPD), and in vitro for rosettes (E, EA, EAC), and lymphocyte blast (phytohemagglutinin - PHA). These tests were repeated every 21-28 days. There was not always agreement between tests in vivo and in vitro. Patients were treated by surgery, irradiation, and cytostatic therapy. Le therapy was started when percent of lymphocytes forming rosettes E in vitro was less than 50%, even in cases when PPD was highly positive (ie giving normal reaction). Of the 51 patients 16 were immuno depressed at the time of diagnosis. All 16 patients received Le therapy. Another seven became immuno depressed later (5 after cytostatic therapy, which did not change PPD results). In all 23 patients, Le therapy caused almost immediate return to normal for rosette forming lymphocyte numbers. Patients showing reduction of lymphocytes T and decrease in tuberculine sensitivity, after Le therapy, demonstrated increase in T lymphocytes and no change in tuberculine (contrary to other published data). Le therapy did not show any side effects. Possible explanation of these results was offered. (11 Refs) (In ITA)

### 46. EFFECT OF LEVAMISOLE ANALOGS ON E-ROSETTE FORMATION BY MITOMYCIN C-TREATED HUMAN LYMPHOCYTES.

Koseki K, Akaza H, Hara T, Kobayashi K, Umeda T, Nijima T, Iwaguchi T

Dept. Urology, Faculty Medicine, Univ. Tokyo, Bunkyu-ku, Tokyo 113, Japan

Gan To Kagaku Ryoho; 8(5):790-795 1981

Incubation of lymphocytes in mitomycin C (MMC) reduced E-rosette formation by human T-lymphocytes, which indicates a possible immunological disadvantage to cancer patients treated by chemotherapy. We investigated whether or not levamisole, known to be a nonspecific immunopotentiator, and its analogs show an E-rosette-restorative effect on the MMC-treated lymphocytes. Levamisole and its analogs, dexamisole, tetramisole, phenylimidazothiazole and paraaminolevamisole, were used at a concentration of 40 ug/ml. When lymphocytes from healthy donors were incubated with MMC (0.01 ug/ml, 0.1 ug/ml, 1.0 ug/ml) for 60 min at 37 C, the rates of E-rosette formation were reduced from 67% to 50, 48, and 43%, respectively. However, when levamisole and its analogs were added to the medium, the percentages of E-rosette formation were higher than those of lymphocytes incubated with MMC alone. Paraaminolevamisole was the most effective in preserving E-rosette formation. Our results indicate that levamisole and its analogs might restore, in cancer patients, the secondary cellular immunity reduced by cancer chemotherapeutic agents. (15 Refs) (In JPN)

## 47. ACUTE NONLYMPHOCYTIC LEUKEMIAS FOLLOWING CHEMOTHERAPY. ULTRASTRUCTURAL STUDY OF ERYTHROBLASTIC CELL LINE AND DISCUSSION OF NUCLEAR ANOMALIES.

Thiery JP, Aurias A, Dumont J, Mazabraud A, Trapet P, Bernard J, Sachs L, Boggs D, Brecher G, Binet JL

Centre de Cytologie Experimentale, 67 rue M. Gunsbourg, 94200 Ivry/Seine, France

Blood Cells; 7(2):341-356 1981

Ultrastructural studies were performed on bone marrow and WBC concentrates of 18 acute nonlymphocytic leukemias following chemotherapy of myeloma (1), Hodgkin's disease (1), non-Hodgkin's lymphoma (5), Ewing's sarcoma (1), and breast carcinoma (10). Radiation was combined with polychemotherapy in some cases. The electron microscopic studies brought out a number of anomalies found in all cells, and described for the erythroblastic cell lines. Anomalies noted in the cytoplasm included siderosomes, iron-containing mitochondria, glycogen spots, various dense inclusions, and nuclear-cytoplasmic asynchronism. Anomalies associated with the nucleus included multinucleated cells, fragility of nuclear membranes, and nuclear clefts and blebs. The structural aspect of nuclear clefts and blebs found in granulocytic and megakaryocytic cell lines suggests a relationship with chromosomal abnormalities, particularly with synaptonemal complexes. Cytogenetic studies in two patients revealed unusual karyotypes which give some credence to this hypothesis. Anticancer alkylating agents carry two reactive groups that can bind to DNA and therefore establish links between two chromosomes. The nuclear clefts and blebs observed may possibly be the morphological expression of the pairing of chromosome segments by alkylating agents. (22 Refs)

## 48. POSSIBILITY OF IMMUNOSTIMULATION IN LUNG CANCER - STUDY OF LYMPHOCYTE SUBPOPULATIONS.

Battista P, Pistone C, Di Perna S, Colamartino P, Di Primio E, Robiao A, Sacco C

Istituto di Patologia Generale, Universita di Chieti, Chieti, Italy

Boll Soc Ital Biol Sper; 57(11):1242-1246 1981

Bronchogenic cancer patients were evaluated before surgery and antiblastic therapy, also for possible future immunotherapy. Before any therapy all patients had rosette Et, Ea, and EAC tests. Tests were repeated after 3 days of levamisole (150 mg/day) treatment, followed immediately by surgery, and 3 days after surgery, too. Controls were 15 healthy persons. Percent rosette values were reported. Control rosettes were: 78% +-3% Et, 28% +-3% Ea, and EAC 12% +-3%. Before levamisole treatment rosettes were: 67.5% Et, 19.6% Ea, and 22.7% EAChu in lung cancer patients. After levamisole treatment they were: 71.5%, 24.5%, and 20.3% respectively. After surgery they were: 71.6%, 24.6%, and 25%, almost unchanged. After surgery rosette Ts were also determined and their value was 4%. Et and Ea rosettes were decreased and EAChu almost normal before levamisole treatment. After levamisole treatment the values were almost normal and they did not change after surgery, except for rather decreased Ts values. Such Ts decrease could be related in lung cancer patients to inhibitors or facilitators, which limit cell mediated immunological activity, through Ts inhibition. (4 Refs) (In ITA)

## 49. GLUCOCORTICOID RECEPTORS AND SENSITIVITY IN LEUKEMIAS.

Ho AD, Hunstein W, Schmid W

Medizinische Universitats-Poliklinik, Hospitalstrasse 3, D-6900 Heidelberg, W. Germany

Blut; 42(3):183-190 1981

Possible correlation between glucocorticoid receptor (GCR) determination and response to treatment in leukemias and lymphomas was studied. GCR determinations were made for leukemic cells from 46 adult leukemia patients and lymphocytes from 18 healthy controls. Leukemias included 17 acute nonlymphoblastic leukemias (ANLL), 4 acute lymphoblastic or undifferentiated leukemias (ALL/AUL), 3 blast crises, 15 chronic lymphocytic leukemias (CLL), and 7 leukemic malignant lymphomas (NHL). Normal lymphocytes expressed 2,312-6,856 GCR/cell (median 3,875). ANLL blasts had 0-15,295 GRC/cell (median 7,250). Two ALL/AUL patients with greater than 5,000 GRC/cell responded to combination therapy including glucocorticoids (GC); two ALL/AUL patients with less than 5,000 GRC/cell showed no response. CLL patients resistant to combination therapy including GC had generally lower GRC than responsive patients, indicating that GCR might have predictive value in CLL. No correlation was found between GCR and in vitro response to dexamethasone. No predictive value for GCR determination was indicated for nonlymphoid leukemias. (28 Refs)

## 50. ALTERATION IN SPLEEN LYMPHOID POPULATIONS ASSOCIATED WITH SPECIFIC AMINO ACID DEPLETION DURING L-ASPARAGINASE TREATMENT.

Distasio JA, Durden DL, Paul RD, Nadji M

Dept. Microbiology, Univ. Miami Sch. Medicine, Miami, FL, 33101

Cancer Res; 42(1):252-258 1982

Treatment with antileukemic asparaginases isolated from Escherichia coli and Erwinia carotovora is accompanied by pronounced toxicity and immunosuppression. The capability of three enzymes to hydrolyze L-glutamine and to limit serum levels of this amino acid as well as asparagine has led investigators to hypothesize that glutaminase activity may be responsible for the side effects observed during treatment. We have isolated a glutaminase-free asparaginase with potent antilymphoma activity from Vibrio succinogenes. With this enzyme, we have demonstrated that asparagine depletion alone does not result in suppression of humoral or cell-mediated responses after immunization with sheep RBC. In contrast, treatment with E coli asparaginase abolishes these immune responses. In this study, we investigated the effects of specific amino acid depletion resulting from asparaginase treatment on spleen histology and lymphocyte populations. Administration by ip injection of 50 IU of E coli asparaginase per day for 4 days resulted in a marked reduction in the size of lymphoid follicles within the spleen concomitant with reduced germinal centers. There appeared to be a significant change in reactivity of the germinal centers, evidenced by a decrease in immunoblasts (B-cells). These findings were confirmed by a sensitive peroxidase-anti peroxidase-staining procedure for Ig-containing cells. Examination of lymphocyte subpopulations within the spleen revealed that there was nearly a 40% decrease in the percentage of SIg-bearing cells accompanied by an increase in the ratio of Thy 1.2-bearing cells. The ratio of Lyt-2 to Lyt-1 cells was unchanged as compared to control animals. The data support the hypothesis that glutamine or glutamine combined with asparagine depletion resulting from the treatment of E coli asparaginase causes a marked decrease in spleen lymphocytes of the B-

cell lineage. In contrast, asparagine deprivation alone, caused by the administration of the glutaminase-free asparaginase from V succinogenes, does not affect spleen histology or lymphocyte marker distribution. Thus, the asparaginase from V succinogenes should serve as an effective antileukemic agent without causing deleterious effects on the immune system. (Author abstract) (34 Refs)

## 51. IMMUNOREGULATION OF HUMAN MYELOPOIESIS.

Verma DS, Spitzer G
Dept. Developmental Therapeutics, Univ Texas M. D. Anderson Hosp. and Tumor Inst., Houston, TX
Cancer Bull; 33(5):218-220 1981

In the light of a proposed hypothesis, the attempt was made to investigate whether the cellular mechanisms that existed for the control of elaboration of colony-stimulating activity (CSA) - molecules essential for proliferation and differentiation of granulocyte-macrophage progenitor cells (GM-CFC) - were the same as those for production of immunoglobulins. Subjects discussed include: monocyte-macrophage and T-lymphocyte interaction for CSA elaboration; mechanisms of monocyte-macrophage and T-lymphocyte interactions for CSA elaboration; clinical application of the experimental data; and monocyte-macrophage inhibition of GM-CFC proliferation by direct cell contact. One of the important findings is that lithium carbonate blocked suppressor T-lymphocyte (TL) activation that would otherwise suppress CSA elaboration. Lithium carbonate was found to be beneficial in ameliorating the neutropenia in a case of preleukemic syndrome, oligoleukemic syndrome, and cyclic neutropenia. It is not beneficial in all types of neutropenic syndromes. The findings suggest lithium carbonate would work successfully only in those patients whose suppressor TL are the etiologic factor for their neutropenia. (12 Refs)

## 52. INDUCTION OF CYTOTOXIC ACTIVITY IN HUMAN LYMPHOCYTES AGAINST AUTOLOGOUS AND ALLOGENEIC MELANOMA CELLS IN VITRO BY CULTURE WITH INTERLEUKIN 2.

Hersey P, Bindon C, Edwards A, Murray E, Phillips G, McCarthy WH
Medical Res. Dept., Kanematsu Memorial Inst., Sydney Hosp., Sydney, Australia
Int J Cancer; 28(6):695-703 1981

THe influence of interleukin 2 (IL2) on the cytotoxic activity of lymphocytes from patients with melanoma against autologous and a variety of allogeneic melanoma cells was studied. These results suggest that lymphocytes from patients with melanoma are primed against autologous antigens in vivo and that provision of a second signal, IL2, in vitro can induce cytotoxicity against the autologous tumor. The cytotoxicity generated against the allogeneic target cells did not appear to have specificity to melanoma. Several results, such as the pattern of cytotoxicity against the target cells and changes in cell surface markers on the lymphocytes during culture, suggesting that cytotoxicity was mediated by activated T cells rather than by natural killer cells. These findings appear to have important implications both in the understanding of tumor-host relationships and for the use of IL2 in therapy. (39 Refs)

## 53. IMMUNOLOGICAL STUDIES IN CHRONIC LYMPHOCYTIC LEUKEMIA. II. NATURAL KILLER- AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY POTENTIALS OF MALIGNANT AND NON-MALIGNANT LYMPHOCYTE SUBSETS AND THE EFFECT OF ALPHA-INTERFERON.

Hokland P, Ellegaard J
Med. afd. II, Aarhus Amtsygehus, 8000 Aarhus C, Denmark
Leuk Res; 5(4/5):349-355 1981

The effector cell potential of chronic lymphocytic leukemic (CLL) subsets was determined in the natural killer (NK) and antibody-dependent cellular cytotoxicity (ADCC) assays. Lymphocyte subpopulations were isolated from peripheral blood obtained from 25 (43-76 yr old) CLL patients. The behavior of CLL cells in NK and ADCC assays was determined. Basic experimental conditions for the assays were determined. When unseparated lymphocytes from CLL patients were tested in NK (21 patients) and ADCC (25 patients) assays and compared to the cytotoxicities of 20 normal donors, the CLL cells were defective in both tests. The behavior of CLL cells in NK assays was defective with or without 1,000 IU alpha-interferon (AIF). The NK and ADCC defects were found mainly in the non-T fraction, while the T cells exhibited subnormal levels of lysis. By depleting the non-T cells of mouse rosette forming cells, a null cell subset was purified that exhibited considerable lysis in the NK test. AIF did not enhance ADCC by unfractionated CLL cells. When the NK activity of three CLL patients were tested against 7 target cell lines with NK sensitivities in normal donors ranging from very low to extremely, the same pattern was retained in the patients, although the addition of AIF tended to diminish the tendency by boosting the NK activity against the resistant lines proportionately more than against the sensitive ones. Compared with lysis by cells from normal donors, the lysis of cells from the patients, was still defective with all cell lines tested. (19 Refs)

## 54. MODULATION OF HUMAN T-CELL DIFFERENTIATION MARKERS BY 12-O-TETRADECANOYLPHORBOL-13-ACETATE.

Nagasawa K, Chechik BE, Gelfand EW, Sengupta S, Letarte M, Mak TW
Ontario Cancer Inst., Toronto, Ontario, Canada
Thymus; 3(4/5):307-318 1981

Extent and sequence of changes in level of seven differentiation markers observed in the human leukemia T-cell line MOLT-3 after incubation with 12-O-tetradecanoylphorbol-13-acetate (TPA) were investigated. Terminal deoxynucleotidyl transferase (TdT) activity decreased rapidly after induction with 1.6 x 10(-8) M TPA. The decrease was not simply a loss of enzyme activity, because the percentage of cells containing TdT measured by single-cell immunofluorescence decreased concomitantly. TPA also induced a rapid, irreversible loss of spontaneous proliferative capacity in the cells. Approx 1 day after the addition of TPA, a linear increase in E-rosette-positive (E+) cells was observed. E+ cells increased to approx 50% of the total between days 3 and 4. TPA also caused a gradual decrease in adenosine deaminase (ADA) activity and HThy-L/ADA (human thymus-leukemia-associated antigen, a low mol wt form of ADA) to approx 30-50% of control values. TPA did not induce any significant changes in ecto-5'-nucleotidase activities, in the proliferative response to phytohemagglutinin, or in the expression of Ia-like antigens. Time kinetics of the changes suggest that the sequence of events induced by TPA is loss of TdT activity, loss of proliferative ac-

tivity and ability to form E-rosettes, and a decrease in ADA (HThy-L/ADA). This sequence appears to follow that proposed for prethymic precursor T-cell differentiation after activation with thymic epithelium. (35 Refs)

### 55. INDUCTION OF MALIGNANT T-LYMPHOBLASTIC CELL LINES MOLT-3 AND JURKAT BY 12-O-TETRADECANOYLPHORBOL-13-ACETATE: BIOCHEMICAL, PHYSICAL, AND MORPHOLOGICAL CHARACTERIZATION.

Nagasawa K, Howatson A, Mak TW
Toronto Cancer Inst., Toronto, Ontario, Canada
J Cell Physiol; 109(1):181-192 1981

Induction of differentiation of human malignant T-lymphoblastic cells by 12-O-tetradecanoylphorbol-13-acetate (TPA) was studied. Cells from leukemic T-cell lines MOLT-3, Jurkat, CCRF-CEM, and CCRF-HSB-2 were exposed to TPA. MOLT-3 cells were stimulated to become E-rosette-positive (E+) in the presence or absence of the DNA synthesis inhibitor 1-beta-D-arabinofuranosylcytosine (ara-C), indicating that the appearance of E+ cells was caused by an inductive, rather than selective, process. TPA induction resulted in the decrease of the marker enzyme terminal deoxynucleotidyl transferase (TdT). Results of exposure to TPA for 1, 6, and 24 hr showed that TPA required only a short time (1 hr or less) for full induction. Jurkat cells responded to TPA in a similar manner to MOLT-3 cells. CCRF-CEM and CCRF-HSB-2 cells did not respond to TPA. Induction of MOLT-3 cells was not affected by the presence of 1 uM concentrations of tumor promotion inhibitors. TPA caused a reduction in vol and morphologic changes in MOLT-3 and Jurkat cells. (43 Refs)

### 56. RAPID EFFECTS OF BCG ON T CELL FUNCTION IN CANCER PATIENTS.

Cannon GB, Reid J, Herberman RB, Connor R, Dean JH, Jerrells T, Perlin E
Dept. Immunology, Litton Bionetics, Incorporated, 5516 Nicholson Lane, Kensington, MD, 20795
Cancer Immunol Immunother; 11(4):265-276 1981

The short-term effects of a single sc injection of BCG on T cell function in cancer patients were studied. Serial blood samples were taken from 48 patients with various cancers and 10 healthy controls. Some patients received 2 x 10(7) or 1 x 10(8) BCG organisms by gun injection. T cell response in all subjects was measured by formation of rosettes with sheep RBC (ERF) and by lymphoproliferative (LP) response to phytohemagglutinin (PHA), purified protein derivative (PPD), and allogeneic cells in mixed lymphocyte cultures. BCG produced a transient increase in ERF and LP response to PPD 3 days after injection. Patients with initially low response to PHA showed an increase on days 3 and 7, while those with initially normal response showed a decrease in response on days 3 and 7. No changes were noted in normal individuals or patients receiving saline or no injections. Apparently BCG has measurable but varied effects on T cell function in some patients. (17 Refs)

### 57. THE EFFECT OF OXIDANT INJURY ON THE LYMPHOCYTE MEMBRANE AND FUNCTIONS.

Kraut EH, Sagone AL
Ohio State Univ. Hosp. N 1025, 410 West 10th Ave., Columbus, OH, 43210
J Lab Clin Med; 98(5):697-703 1981

We have studied the effect of oxidant stress on the lymphocyte membrane and lymphocyte functions. Lymphocyte cultures were incubated with xanthine oxidase and xanthine, an enzyme system known to generate several highly reactive oxygen compounds. We demonstrated that these lymphocytes were viable after exposure to an in vitro oxidant stress. However, there was a marked reduction in their ability to bind sheep RBCs and to form caps after Concanavalin A stimulation. These lymphocytes also demonstrated a delay in phytohemagglutinin-induced lymphoblastic transformation, with max response occuring at 5 days instead of 3 days. Catalase, a hydrogen peroxide scavenger, protected lymphocytes from this injury, implicating hydrogen peroxide as the causative agent. Another lymphocyte membrane-related function, the ability to stimulate or respond in mixed leukocyte culture, was not impaired after oxidant injury. These results demonstrate that after in vitro oxidant injury, lymphocytes may have alterations in the cell membrane and impaired function. (Author abstract) (24 Refs)

### 58. IMMUNOPHARMACOLOGICAL EFFECTS OF IRRADIATION.

Serrou B, Rey A
Laboratoire d'Immunopharmacologie des Tumeurs, INSERM U 236, ERA-CNRS no. 844, Centre Paul Lamarque, B.P. 5054, F-34033 Montpellier Cedex, France
Cancer Immunol Immunother; 11(4):239-242 1981

Effects of irradiation on immune response are reviewed. Localized irradiation has a depressive effect on T lymphocytes, monocytes, and null cells. Decreases in mitogen response, natural killer activity, and antibody- and phytohemagglutinin-induced cytotoxic response are produced. B lymphocyte response is apparently not affected, at least in the short term. Animal studies indicate a decrease in specific T cell cytotoxicity against tumor antigens, but the decrease has not been demonstrated in man. Preliminary results show that autologous rosette formation decreases after irradiation, indicating change in a nonsuppressor T cell population. Stress effects have been produced in animals at doses ranging from 0.12 to 16 gray local irradiation. Irradiation may combine with other agents to promote development of certain cancers. Some controversial studies suggest that irradiation itself may promote metastasis. The negative effects of irradiation may be reducible or avoidable by the use of other appropriate agents such as BCG. Clinical studies are required to determine the effects of irradiation on humans. (49 Refs)

## OTHER RELATED STUDIES

### 59. GROWTH OF HUMAN NORMAL AND LEUKEMIC T CELLS: T-CELL GROWTH FACTOR (TCGF) AND THE ISOLATION OF A NEW CLASS OF RNA TUMOR VIRUSES (HTLV).

Gallo RC, De The, Lajtha L, Van Bekkum DW, McCulloch EA, Greaves MJ, Seligmann M, Brecher G, Shohet SB, Bessis M, Sachs L
Lab. Tumor Cell Biology, NCI, NIH, Bethesda, MD, 20205
Blood Cells; 7(2):313-329 1981

Previous studies have indicated that T-cell growth factor (TCGF) is the physiological growth promoter in the immune response of T-lymphocytes, acting as the second signal (after antigen) in the immune response. A summary is presented of information on proliferation of normal T-cells in a previously described liquid suspension culture and proliferation of several

new cell lines from patients with particular types of T-cell leukemias and lymphomas. Information on the new type-C virus designated HTLV is also summarized. Neoplastic T cells from patients with cutaneous T-cell leukemias and and lymphomas, eg Sezary syndrome and mycosis fungoides, were grown routinely with the use of purified TCGF free of phytohemagglutinin and of lymphokines other than TCGF. The neoplastic T cells responded directly to TCGF without prior in vitro activation with antigen or lectin as is necessary with normal T cells. Thus, transformed mature T cells already express TCGF receptors. HTLV were isolated from some of these new cell lines. Evidence is presented to indicate these may be the first unambiguous isolates of RNA tumor viruses from humans. These new viruses are easily distinguished from all previously isolated viruses from animals. Antibodies in sera of some patients with these diseases specifically react with proteins of these viruses. (11 Refs)

## 60. ROLE OF VIRUSES IN THE ETIOLOGY OF NATURALLY OCCURRING FELINE LEUKEMIA.

**Essex M, Grant CK, Cotter SM, Hardy Jr WD**
**Dept. Microbiology, Harvard Sch. Public Health, 665 Huntington Ave., Boston, MA, 02115**
**Haematol Blood Transfus; 26:483-487 1981**

The biology and natural history of the feline retroviruses and the diseases they cause are reviewed. The feline leukemia viruses (FeLV) cause several forms of leukemia and lymphoma that occur at different rates in different geographic areas; no specific association between naturally occurring disease and any strain(s) of any subgroup(s) has been demonstrated. FeLVs are replication competent and cause no visible pathology in infected cultured cells. FeLVs are transmitted in a contagious manner. Approx 2-5% of infected cats become persistently viremic, and one-fourth to one-third of these animals develop leukemia (the other develop infectious peritonitis, septicemia, or glomerulonephritis). Both leukemic and persistently viremic cats release large amounts of infectious FeLV in their saliva. FeLV appears to play an important role in the etiology of 'virus-negative' leukemia in cats; an understanding of the mechanism of this phenomenon may help us to explain human leukemias that occur in individuals that do not harbor replicating virus. FeLV particles contain seven distinct proteins, several of which have greater than 1 antigenic determinant and all of which induce immune responses in cats to some degree. The feline oncornavirus-associated cell membrane antigen (FOCMA) is found on lymphoma and/or leukemia cells, and the immune response to it is correlated with protection against development of leukemia and lymphoma. Two general classes of tumor- and transformation-specific antigens have been found. (39 Refs)

## 61. RELATIONSHIP OF THE FELINE ONCORNAVIRUS ASSOCIATED CELL MEMBRANE ANTIGEN TO A FELINE SARCOMA VIRUS ENCODED POLYPROTEIN.

**Snyder HW, Dutta-Choudhury M, Hardy Jr WD**
**No affiliation given**
**Haematol Blood Transfus; 26:488-491 1981**

Using immunoaffinity chromatography on a column of Sepharose containing bound IgG from cat anti-feline oncornavirus-associated cell membrane antigen (FOCMA) serum, a 70,000-dalton protein was isolated from lysates of mink cells transformed by the Gardner-Arnstein strain of feline sarcoma virus (GA-FeSV). This result was unanticipated because previous evidence had suggested that FOCMA was associated with the much larger (95,000 dalton) gag-x fusion protein in these cells. The GA-FeSV gag-x protein was also isolated by virtue of its binding to anti-FeSV antibodies on a different affinity column. Preliminary biochemical characterization of the 70,000-dalton protein from both GA-FeSV-transformed mink fibroblasts and feline lymphosarcoma cells showed no differences between them. The gag-x protein was di stinguishable by labelling with 32P-orthophosphate, association with protein kinase activity, and its precipitation ability with antibodies in a hyperimmune antiserum to FeLV structural proteins. It is hypothesized that FOCMA may actually be a family of antigens, not all of which cross-react with FeSV polyprotein antigens. (21 Refs)

## 62. IDENTIFICATION OF ANTIGENIC DETERMINANTS UNIQUE TO THE SURFACES OF CELLS TRANSFORMED BY EPSTEIN-BARR VIRUS.

**Kintner C, Sugden B**
**Div. Biology, California Inst. Technology, Pasadena, CA, 91125**
**Nature; 294(5840):458-460 1981**

Four monoclonal antibodies (anti-EBVCS) that detect antigenic determinants unique to the surfaces of Epstein-Barr virus (EBV)-transformed cells but are not associated with virus production were isolated. Cell lines transformed in vitro or those transformed in vivo but not associated with Burkitt's lymphoma bound anti-EBVCS strongly, whereas cell lines from patients with Burkitt's lymphoma bound them at intermediate levels or not at all. When untreated lymphocytes and lymphocytes exposed to EBV, Concanavalin A, and pokeweed mitogen were assayed, only EBV-exposed lymphocytes expressed EBVCS determinants, which were detectable within 48 hr after infection. Assay of unseparated populations of EBV-exposed primary lymphocytes and immunoglobulin-positive and -negative populations indicated that those cells which express EBVCS determinants are separated as B cells along with those which express the EBV-induced nuclear antigen and that the two antigen-expressing populations are overlapping and may be identical. A polypeptide with an apparent mol wt of 45,000 was precipitated from an EBVCS-positive cell line and was likely to be the molecule which carries EBVCS determinants. The results indicate that EBVCS determinants are expressed at reduced levels on cell lines established from Burkitt's lymphoma patients relative to expression on other EBV-transformed cell lines. EBVCS determinants are among possible determinants recognized by autochthonous, cytotoxic T cells specific for EBV-transformed cells and may therefore be equivalent to lymphocyte determined membrane antigen (LYDMA); this possibility was supported by the finding that EBVCS and LYDMA were expressed with the same time course in lymphocytes infected with EBV in vitro. If the EBVCS determinants are used by cytotoxic T cells to identify their targets, reduced expression of EBVCS on Burkitt's lymphoma cell lines is consistent with these tumor cells having been selected in vivo to survive that cytotoxic response. (18 Refs)

## 63. DIFFERENTIAL EXPRESSION OF MURINE LEUKEMIA ANTIGEN ON L1210 PARENTAL AND DRUG-RESISTANT SUBLINES.

**Strzadala L, Opolski A, Radzikowski C, Mihich E**
**Inst. Immunology and Experimental Therapy, Czerska 12, 53-114, Wroclaw, Poland**
**Cancer Res; 41(12):4934-4937 1981**

The differential expression of surface antigens on L1210 leukemia DBA/2 and drug-resistant L1210 sublines was investigated. In direct cytotoxic test, the anti-L1210/v alloantiserum

reacted more strongly with subline cells than with parental cells. Absorption of the antiserum with Gross cellular surface antigen-positive AKR leukemia (AKSL-4) cells led to a much greater difference in this reactivity. Quantitative absorption experiments revealed that the drug-resistant sublines had 5x higher absorption capacity than did the parental line. After complete absorption of antibodies against murine leukemia virus-related antigens, the anti-L1210/v alloantiserum still reacted with L1210 cells. This cytotoxicity could be removed after absorption with C3H mammary tumor (MAC-1) cells but not with normal C3H lymphocytes. These results provide evidence that the major cytotoxic activity of the antiserum against L1210 and L1210 subline cells was due to antibodies against murine mammary tumor virus-related antigen and that the drug-resistant sublines of leukemia L1210 have higher quantitative expression of mammary leukemia antigens. (Author abstract) (15 Refs)

## 64. EFFECTOR CELLS IN NATURAL CYTOTOXICITY AGAINST HUMAN BLADDER CANCER CELL LINES.

**Bloom ET, Dunsworth-Browne M, Durkos-Smith D**
**GRECC 691/11G, Veterans Admin. Wadsworth Medical Center, Los Angeles, CA, 90073**
**Urol Res; 9(5):219-225 1981**

Mononuclear cells were obtained from normal donors and from patients with nonmalignant genitourinary diseases, bladder cancer, and other cancers. The cells were tested for cytotoxicity after depletion of Fc-receptor-bearing (FcR+) cells by monolayer immune complex fractionation or the RBC-antiRBC monolayer technique. FcR+ cell depletion significantly decreased cytotoxicity of effector cells (ECs) against transitional cell carcinoma, colon carcinoma, and amnion target cells in a 40-hr assay. No bladder cancer-specific cytotoxicity was detected. Cultured ECs from normal donors were positive for natural killing (NK) against transitional cell carcinoma and amnion cells. The NK activity appeared to involve FcR- T and B cells since FcR+ cells were frequently undetectable. Monocytes did not play a significant role in NK. (21 Refs)

## 65. CHARACTERISTICS AND ACTION OF THE CONCANAVALIN A (CON A)-INDUCED SUPPRESSOR CELLS IN HUMAN PERIPHERAL BLOOD LYMPHOCYTES.

**Toge T, Yanagawa E, Nakanishi K, Kohno H, Yamada Y, Hattori T**
**Dept. Surgery, Res. Inst. Nuclear Medicine and Biology, Hiroshima Univ., Kasumi, Hiroshima 734, Japan**
**Gan To Kagaku Ryoho; 8(5):802-808 1981**

After treatment with Con A, peripheral blood lymphocytes from both normal donors and cancer patients contained Con A-induced suppressor cells which depress the proliferative response of lymphocytes from normal donors. Con A-induced suppressor cells were present among E-rosette forming cell s. The activities of these cells were apparent when added on day 0 of responder cell cultures. In our assay system, allo-antigen-induced proliferation as well as mitogen-induced proliferation was depressed by Con A-activated cells. In esophageal, colorectal and gastric cancer patients, a significant increase in Con A-induced suppressor cell activity as compared with normal donors was observed, whereas in patients with breast cancer, there was no such increase in activity. In patients with advanced gastric cancer, increased suppressor cell activity was also found, and it decreased significantly after resection of the tumors. The suppressor mechanisms may be of major importance in governing the outcome of antitumor responses. (25 Refs) (In JPN)

## 66. SUPPRESSION OF NATURAL KILLER (NK) ACTIVITY BY SPLENIC ADHERENT CELLS OF LOW NK-REACTIVE MICE.

**Riccardi C, Santoni A, Barlozzari T, Cesarini C, Herberman RB**
**Inst. Pharmacology, Univ. Perugia, 06100 Perugia, Italy**
**Int J Cancer; 28(6):811-818 1981**

Adherent cells with the ability to inhibit NK activity were found in the spleens of young 8-wk-old SJL/J mice. Such suppressor cells were also found in the spleens of other low-NK-reactive strains, but not in the spleen of age-matched high-NK-reactive strains. These suppressor cells had the characteristics of macrophages, since they were plastic- and nylon-adherent, phagocytosed latex and iron particles, and were resistant to treatment with anti-Thy-1.2 serum plus complement. Their inhibitory activity appeared to be due to their production and/or release of soluble suppressive factor(s). Their suppressor activity was similar to that of pyran copolymer-activated macrophages, which were previously shown to be suppressive for cytotoxicity by NK cells. We suggest here that macrophages may be involved in the physiological regulation of NK activity and may contribute to the low NK activity in some strains of mice. (Author abstract) (25 Refs)

## 67. PRODUCTS OF THE IMMUNE SYSTEM AS IMMUNOMODULATORS.

**Sakiyama Y**
**Dept. Pediatrics, Hokkaido Univ. Sch. Medicine, Hokkaido, Japan**
**Nippon Rinsho; 39(4):156-162 1981**

Research findings concerning the immunomodulating properties of transfer factor, thymus factors, lymphokines, and interferon were discussed. One particular property of transfer factor was imputing in vitro cytotoxic effects onto tumor cells. Of the thymus factors discussed (ie, thymosin, circulating thymic factor, thymic humoral factor, thymopoietin, and thymic epithelium supernatants), circulating thymic factor was found to have receptors observed in T-cells that were precultured with acute leukemia T-cell strains and normal human peripheral blood without the serum. Lymphokine activity has been observed in diseases exhibiting abnormal lymphocyte proliferation such as Hodgkin's disease, lymphoma, and myeloma, and a ntitumor activity of lymphokines was thought to be related to that of interferon. Antitumor effects of interferon have been observed in cases of osteosarcoma, lymphoma, melanoma, breast cancer, pharyngeal papilloma, and multiple myeloma. (20 Refs) (In JPN)

## 68. HUMAN CUTANEOUS T CELL LYMPHOMA AND LEUKEMIA CELL LINES PRODUCE AND RESPOND TO T CELL GROWTH FACTOR.

**Gootenberg JE, Ruscetti FW, Mier JW, Gazdar A, Gallo RC**
**Lab. Tumor Cell Biology, NCI, Bethesda, MD, 20205**
**J Exp Med; 154(5):1403-1418 1981**

Constitutive production of T cell growth factor (TCGF) was found in three cell lines derived from mature T cells of patients with cutaneous T cell lymphoma-leukemias (CTCL). TCGF produced by tumor cells (L-TCGF) was found in the culture medium and also bound to the cell membrane. TCGF produced by normal peripheral blood leukocytes (N-TCGF) was adsorbed by normal T lymphocytes that had been activated by phytohemagglutinin (PHA) and by the three CTLC cell lines. N-TCGF was not adsorbed by nonactivated normal T lymphocytes or by other human leukemic cell types. TCGF was eluted from the cell membranes of CTLC and PHA-acti-

vated normal T cells using an acid glycine buffer, but could not be eluted from nonactivated cells. TCGF stimulated the growth of activated normal T cells, TCGF-dependent CTCL cells, and TCGF-independent CTCL cells. L-TCGF and N-TCGF had the same biological activity. Production of and response to TCGF by the same cells (autostimulation) apparently is characteristic of some, but not all neoplastic cell populations and enhances proliferation of such cells. (30 Refs)

## 69. SPONTANEOUS RELEASE OF A FACTOR WITH PROPERTIES OF T CELL GROWTH FACTOR FROM A CONTINUOUS LINE OF PRIMATE TUMOR T CELLS.

**Rabin H, Hopkins RF, Ruscetti FW, Neubauer RH, Brown RL, Kawakami TG**
**Biological Carcinogenesis Program, Frederick Cancer Res. Center, Frederick, MD, 21701**
**J Immunol; 127(5):1852-1856 1981**

A continuous lymphoid cell line had been previously established from a gibbon with spontaneous lymphosarcoma. This cell line, designated as MLA144, when tested after several yr in culture was shown to release spontaneously a factor biologically and biochemically similar to human T cell growth factor (TCGF). Conditioned media (CM) from MLA144 cells support growth and DNA synthesis of T cells from humans, several other species of primates, and also from mice and rabbits. The activity in the MLA144 CM is resistant to 60 C and to low and high pH, has a mol wt, as determined by gel filtration, of 21,500, elutes from DEAE-cellulose at 0.04 to 0.06 M sodium phosphate buffer, pH 7.6, and has an isoelectric point of about 6.45. Surface-marker analysis of MLA144 cells by rosetting techniques indicates that they are T cells lacking in the receptor for the Fc portion of IgG. The release of TCGF by MLA144 cells should have practical value in terms of ease of TCGF production and should be of great help in the facilitation of studies on the cell biology and molecular biology of TCGF production. (Author abstract) (19 Refs)

## 70. STIMULATOR ACTIVITY OF PHA-LCM FOR NORMAL HUMAN HEMOPOIETIC PROGENITORS AND LEUKEMIC BLAST CELL PRECURSORS: SEPARATION BY ISOELECTRIC FOCUSING.

**Fauser AA, Messner HA**
**Dept. Medicine, Ontario Cancer Inst., Toronto, Ontario M4X 1K9, Canada**
**J Supramol Struct Cell Biochem; 15(1):41-48 1981**

Factors in medium conditioned by leukocytes in the presence of phytohemagglutinin (PHA-LCM) that promote growth of human hemopoietic progenitors and leukemic blast cell precursors (LBC) were studied. PHA-LCM was prepared from peripheral blood of a patient with hemochromatosis. Growth-promoting factors in PHA-LCM were separated by isoelectric focusing. Nonadherent, mononuclear bone marrow cells from normal individuals and mononuclear, E-rosette-depleted peripheral blood cells from patients with acute myeloblastic leukemia were used as appropriate targets for the fractions. Factors promoting growth of pluripotent hemopoietic, erythroid, and granulocytic precursors had activity profiles of pH 5.0-6.5; these factors could be partially separated from a factor promoting LBC, which had a broader profile at pH 5.5-7.5, but not from each other. Isolation of growth-promoting factors with specificity for LBC would facilitate cloning of leukemic cells and permit study of the relationships between normal and leukemic hemopoiesis. (23 Refs)

## 71. THE BINDING OF BCG-ACTIVATED MACROPHAGES TO TUMOR TARGETS STIMULATES SECRETION OF CYTOLYTIC FACTOR.

**Johnson WJ, Whisnant CC, Adams DO**
**Dept. Pathology, Duke Univ. Medical Center, Durham, NC, 27710**
**J Immunol; 127(5):1787-1792 1981**

The binding of neoplastic targets and the secretion of a potent cytolytic protease (CF) by BCG-activated macrophages have previously been shown to be independent functions, both of which are necessary for completion of macrophage-mediated cytolysis. The present studies demonstrate that secretion of CF is triggered by the binding of neoplastic targets to BCG-activated macrophages. The binding of tumor targets, but not of normal lymphocytes, resulted in enhanced secretion of CF from BCG-activated macrophages, although not from macrophages elicited by thioglycolate broth. Dead or metabolically inactive tumor targets, as well as membrane preparations of tumor targets, induced secretion of CF from BCG-activated macrophages. The blocking of macrophage-target binding with a porous filter prevented augmented secretion of CF. Appreciable secretion of CF occurred in as little as 30 min after addition of tumor targets to BCG macrophages. Binding did not induce a generalized increase in secretion of neutral proteases by BCG macrophages, since secretion of plasminogen activa. was actually decreased after the binding of P815 targets. The data suggest the selective binding of BCG-activated murine macrophages to neoplastic targets triggers the secretion of a potent CF. (Author abstract) (33 Refs)

## 72. SUPPRESSION OF LYMPHOCYTE PROLIFERATION BY HUMAN TUMOR CELLS GROWN IN SHORT TERM CULTURES.

**Lafferty WE, Kempf RA, Goodwin JS**
**(c/o Goodwin) Dept. Medicine, Univ. New Mexico Sch. Medicine, Albuquerque, NM, 87131**
**J Clin Lab Immunol; 6(2):157-163 1981**

The effect of short-term cultures of human tumor cells (less than 10 passages) added to mitogen- and alloantigen-stimulated cultures of peripheral blood monocyte cells (PBMC) on the proliferative responses of PBMC from natural donors was studied. At 1/10 and 1/100 tumor cell/PBMC ratios, only 1/7 tumor cell lines, (a melanoma) caused no suppression of phytohemagglutinin-stimulated cultures. Tumor cells were 50 x more suppressive than normal human fibroblasts. Similar results were obtained using concanavalin A. In mixed lymphocyte cultures, 1/10 tumor cell/lymphocyte ratios resulted in 66-85% suppression, while 1/100 tumor cell/lymphocyte ratios caused 43-66% suppression. Suppression of 3H thymidine incorporation of stimulated lymphocytes by tumor cell line T was evident throughout the 120 hr culture. PBMC recovery and viability were comparable after culture with and without tumor cell T. The percent suppression of 3H thymidine incorporation did not increase as the concentration of 3H thymidine decreased. Glass wool adherent cells were not required for suppression. The inclusion of the prostaglandin-inhibitor indomethacin had no effect on 3H thymidine incorporation by PBMC cultured with tumor cells. Mitomycin C completely abrogated the suppression by tumor T cells while irradiation with 1,000, 2,000, and 3,000 rad had little effect. Tumor cell line T inhibited 3H thymidine incorporation only when incubated in the same chamber with PBMC, not when separated from PBMC by a cell-impermeable membrane. Tumor cell line U, however caused 68% suppression when incubated in the same chamber with PBMC, and 40.4% inhibition across a cell-impermeable membrane. (27 Refs)

## 73. A RAPID METHOD FOR THE ISOLATION OF METASTASIZING TUMOUR CELLS FROM INTERNAL ORGANS WITH THE HELP OF ISOPYCNIC DENSITY-GRADIENT CENTRIFUGATION IN PERCOLL.

**Boulet K, Ruffmann R, Altevogt P, Schirrmacher V**
**Institut fur Immunologie und Genetik, Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, 6900 Heidelberg, W. Germany**
**Br J Cancer; 44(3):356-362 1981**

Metastasizing tumor cells from a DBA/2 mouse T-cell lymphoma could be separated from the invaded tissue by isopycnic centrifugation in continuous Percoll density gradients. The metastasizing tumor cells from spleen, liver and lung, derived from a cloned lymphoma-cell line, showed a buoyant densi ty in Percoll of 1.060 +-0.010. They could be separated from the host tissue, which had a higher buoyant density in the case of the spleen cells or a lower density in the case of the dead liver or lung tissue. The separated tumor cells as removed from the gradients were viable, and could be analyzed by in vitro and in vivo assays. The separation procedure did not affect the expression by the tumor cells of TATAs and H-2 antigens. Furthermore, the method seemed to be applicable to the separation of human tumor cells from mononuclear cells prepared from blood samples of tumor patients by Ficoll centrifugation. (Author abstract) (18 Refs)

* U.S. GOVERNMENT PRINTING OFFICE: 1982—361-847/114

# AUTHOR INDEX WITH CITATION NUMBERS


Adams DO 71
Advani SH 6
Aisenberg AC 10
Akaza H 46
Albrecht R 28
Altevogt P 73
Antropoli L 45
Aurias A 47
Babusikova O 1
Bagnara GP 7
Barlozzari T 66
Bartlett SP 34
Battista P 48
Benson NA 20
Bernard J 47
Bessis M 59
Biagini G 7
Bindon C 52
Binet JL 4
Binet JL 47
Bloch KJ 10
Bloom ET 64
Bodega E 4
Boesen AM 2
Boggs D 47
Bonsi L 7
Borowitz MJ 13
Borrelli G 45
Bosslet K 73
Braylan RC 20
Brecher G 47
Brecher G 59
Brown RL 69
Burton RC 34
Butcher EF 41
Cannon GB 56
Cap J 1
Caraux J 24
Catovsky D 5
Catovsky D 9
Cawley JC 35
Cesarini C 66
Chechik BE 54
Cherchi M 5
Christen C 28
Clancy RL 43
Colamartino P 48
Comis M 7
Connor R 56
Corrales A 19
Cotter SM 60
Croker BP 13
De The 59
Dean JH 56
Desplaces A 24
Di Perna S 48
Di Primio E 48
Diez RA 44
Dighiero G 4
Dinshaw KA 6
Distasio JA 50
Doe WF 43
Dorf ME 27
Dufer J 24
Dumont J 47
Dunsworth-Brown 64
Durden DL 50
Durkos-Smith D 64
Dutta-Choudhury 61
Edwards A 52
Ellegaard J 2
Ellegaard J 3
Ellegaard J 53
Ellims PH 15
Essex M 60
Esteve C 24
Estevez ME 44
Fanger MW 35
Fauser AA 70
Finnegan A 32
Fixa B 26
Foltinova A 1
Forbes IJ 39
Forster HK 28
Fridland DIu 12
Gallo RC 59
Gallo RC 68
Gan TE 15
Garagiola DM 36
Gawande SR 6
Gazdar A 68
Gelfand EW 54
Gennarelli E 45
Girard MF 28
Giuliano AE 30
Gnasso P 45
Goldstein G 9
Golub SH 30
Gomez R 5
Gonzalez M 19
Good RA 37
Goodwin JS 72
Gootenberg JE 68
Gopal R 6
Grant CK 60
Greaves MF 9
Greaves MJ 4
Greaves MJ 59
Gudat F 28
Hammerling U 33
Hansen JA 29
Hara T 46
Hardy Jr WD 60
Hardy Jr WD 61
Hariri G 9
Hasui K 22
Hattori T 65
Herberman RB 56
Herberman RB 66
Hernandez F 19
Hersey P 52
Ho AD 49
Hokland P 2
Hokland P 3
Hokland P 53
Hollander N 41
Hopkins RF 69
Howatson A 55
Huard TK 36
Hunstein W 49
Iacopino P 7
Ikeda S 16
Ikehara S 37
Ito K 14
Iwaguchi T 46
Jankowiak S 42
Jansen J 18
Jerabek L 41
Jerrells T 56
Johnson WJ 71
Kaplan G 38
Karavodin LM 30
Kawakami TG 69
Kay NE 17
Kempf RA 72
Kimura S 33
Kintner C 62
Kita K 8
Kobayashi K 46
Kohno H 65
Koseki K 46
Kraut EH 57
Kruth HS 20
Kumar V 34
Kung P 9
Lafferty WE 72
Lajtha L 4
Lajtha L 59
Lassen BL 2
Ledesma M 19
Letarte M 54
Liu Y 33
LoBuglio AF 36
Lopez Borrasca 19
Loseva MI 12
Ludwig C 28
Lunzer DG 37
Lydyard PM 35
Maeda K 14
Mak TW 54
Mak TW 55
Marani M 7
Markowska J 42
Martin PJ 29
Marzo C 45
Matutes E 5
Mazabraud A 47
McCarthy WH 52
McCulloch EA 4
McCulloch EA 59
McGrath MS 41
Messner HA 70
Metzgar RS 13
Mier JW 68
Mihich E 63
Minato K 11
Misikova Z 1
Modak MJ 37

Munck A. 21
Murray AW. 39
Murray E. 52
Nadji M. 50
Nadkarni JJ. 6
Nagasawa K. 54
Nagasawa K. 55
Nair CN. 6
Nakanishi K. 65
Nakayama E. 33
Nasu K. 8
Neri A. 7
Neuhauer RH. 69
Niijima T. 46
Nishikori M. 8
Nobile F. 7
Nourse VA. 20
Nowinski RC. 29
Obrecht JP. 28
Oken MM. 17
Olstad R. 38
Omary MB. 31
Opolski A. 63
Owen FL. 32
Pahwa RN. 37
Pang RH. 40
Pasquinucci S. 45
Paul RD. 50
Perlin E. 56
Phillips G. 52
Pillemer E. 41
Pistone C. 48
Powell RG. 35
Pucci A. 43
Rabin H. 69
Radzikowski C. 63
Rao J. 9
Reid J. 56
Revoltella. 4
Rey A. 24
Rey A. 58
Riccardi C. 66
Robb RJ. 21
Robino A. 48
Rodriguez-Valve. 25
Ronco F. 7
Rouse RV. 41
Rucheton M. 24
Ruffmann R. 73
Ruscetti FW. 68
Ruscetti FW. 69
Sacco C. 48
Sachs L. 4
Sachs L. 47
Sachs L. 59
Sagone AL. 57
Saito H. 11
Saiz-Garcia F. 25
Sakiyama Y. 67
San Miguel J. 19
Santoni A. 66
Satam MN. 6
Sato E. 22
Schirrmacher V. 73
Schmid W. 49
Scollay RG. 41
Seligmann M. 4
Seligmann M. 59
Sen L. 44
Sengupta S. 54
Serrou B. 24
Serrou B. 58
Severi B. 7
Shimatani N. 23
Shimoyama M. 11
Shirakawa S. 8
Shohet SB. 59
Siadak AW. 29
Simm S. 42
Sirsat SM. 6
Smith KA. 21
Snyder HW. 61
Spitzer G. 51
Stevens SK. 41
Strzadala L. 63
Sugden B. 62
Tada N. 33
Takiuchi Y. 8
Tatsumi E. 8
Thierry C. 24
Thiery JP. 47
Toge T. 65
Tomaszkiewicz T. 42
Tosner J. 26
Trapet P. 47
Trowbridge IS. 31
Uchino H. 8
Umeda T. 46
Valente L. 39
Valles H. 24
Valvassori L. 7
Van Bekkum DW. 59
Van der Weyden. 15
Vejbora O. 26
Verbi W. 9
Verma DS. 51
Vilcek J. 40
Vitiello N. 45
Watanabe S. 11
Wechsler A. 5
Weissman IL. 41
Whisnant CC. 71
Wilkes BM. 10
Winn HJ. 34
Worman CP. 35
Yagi Y. 22
Yamada Y. 65
Yamaguchi N. 14
Yanagawa E. 65
Yip YK. 40
Zagury D. 24
Zalewski PD. 39
Zwaan FE. 18

# Keep Up with the Cancer Literature

## Each Month
## You Can Receive Abstracts
## Covering Your Specialty Area

- This convenient service — called Auto SDI* — is as near as your nearest biomedical library. Discuss your research interests with the librarian who will design an appropriate search strategy.
- Abstracts of the latest published literature are searched automatically each month and those related to your interests are delivered to you on a regular basis.
- The abstracts you receive are selected from more than 4,000 monthly entries made into CANCERLIT — the extensive cancer literature data base of the National Cancer Institute.

## Talk With Your Librarian
## About the Auto SDI Service TODAY.

*Auto SDI stands for Automatic Selective Dissemination of Information. It is a service provided to you, at minimal cost, by the International Cancer Research Data Bank (ICRDB) — a part of the National Cancer Institute.

# VIDEOTAPES

## ON CURRENT TOPICS IN CANCER RESEARCH

A pilot project of the International Cancer Research Data Bank (ICRDB) Program of the National Cancer Institute

*Three series are available . . .*

### THE RELATION OF CARCINOGEN ACTION ON DNA TO CELL TRANSFORMATION

| | | |
|---|---|---|
| PETER MAGEE<br>Fels Research Institute | *Keynote Address* | #VK01<br>28 min. |
| JAMES K. SELKIRK<br>Oak Ridge National Laboratories | *Metabolic Activation and Macromolecular Binding of Chemical Carcinogens* | #VK02<br>51 min. |
| PHILIP C. HANAWALT<br>Stanford University | *Cellular Responses to Damaged DNA* | #VK03<br>54 min. |
| CHARLES HEIDELBERGER<br>University of Southern California | *Mutagenesis and Oncogenic Transformation of Mouse Embryo Cells* | #VK04<br>54 min. |
| FRED RAPP<br>Milton S. Hershey Medical Center | *The Interaction of Herpesviruses and Host Cells Leading to Latency or Transformation* | #VK05<br>52 min. |
| | *Panel Discussion* | #VK06<br>31 min. |

### MECHANISMS OF METASTASIS

| | | |
|---|---|---|
| ISAIAH FIDLER<br>Frederick Cancer Research Center | *The Heterogeneous Nature of Cancer Metastasis and Implications for Therapy* | #VB01<br>47 min. |
| GEORGE POSTE<br>Smith, Kline and French Laboratories | *Phenotypic Analysis of Metastatic Cell Populations* | #VB02<br>42 min. |
| LANCE LIOTTA<br>National Cancer Institute | *Tumor Cell Invasion of Basement Membranes and Extracellular Matrices* | #VB03<br>33 min. |
| EVERETT SUGARBAKER<br>Miami Cancer Institute | *Some Clinical Characteristics of Metastasis in Man* | #VB04<br>41 min. |

### AUTOMATED CYTOLOGY

| | |
|---|---|
| Part One: Principles and Techniques | #VB05<br>56 min. |
| Part Two: Biological Applications | #VB06<br>52 min. |

VIDEOTAPES ON CURRENT TOPICS IN CANCER RESEARCH are in the 3/4" U-matic format and can be played on video equipment which accepts the NTSC standard (the standard for videotapes produced in the U.S.).

The videotapes are available on a loan basis. If you would like to schedule viewing for your group, or for more information, please write to:

Cancer Information Dissemination and Analysis Center (CIDAC)
Franklin Research Center
20th and Benjamin Franklin Parkway
Philadelphia, PA 19103

Please specify three choices for viewing dates, and the tapes desired.

# NOW

# Your Complimentary Copy of

# The Latest DIRECTORY OF CANCER RESEARCH INFORMATION RESOURCES

*Just Return the Form at the Bottom of this Page*

This Directory is Your Guide to the Following Information Sources:

COMPUTERIZED CANCER INFORMATION available through biomedical libraries

PRIMARY JOURNALS containing cancer-related articles

SECONDARY PUBLICATIONS such as abstract bulletins, indexes, bibliographies, etc.

INFORMATION ON PROJECT DESCRIPTIONS AND FUNDING SOURCES

ORGANIZATIONS that provide fellowships, grants, and other support of cancer research, as well as organizations that conduct research

REGISTRIES of cancer patient data

LIBRARIES with special collections of cancer-related literature

CLASSIFICATIONS used to categorize and index cancer information

SPECIAL COLLECTIONS of cancer-related materials

AUDIOVISUAL MATERIALS dealing with cancer

---

Request for **COMPLIMENTARY DIRECTORY:**
(*Print Clearly* for use as mailing label)

Name: _____

Address: _____

_____

City/State/Zip: _____

Country: _____

*Mail to:*
Directory Request
ICRDB Program
National Cancer Institute
Westwood Building Room 10A18
Bethesda, Maryland 20205

**U.S. DEPARTMENT OF COMMERCE**
**National Technical Information Service**
5285 Port Royal Road
Springfield, Va. 22161

OFFICIAL BUSINESS

Penalty for Private Use, $300

**PRINTED MATTER**

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF COMMERCE
COM-211

THIRD CLASS
BULK RATE

U.S.MAIL

CB-17

**CANCERGRAMS are distributed for the International Cancer Research Data Bank (ICRDB) by the National Technical Information Service (NTIS). CANCERGRAMS are available from NTIS on a standing order basis at $2 each for North American Continent addressees and $3 each for other addressees. An NTIS deposit account is required. For a list of subject categories or other information, please write to:**

**Subscription Section**
**National Technical Information Service**
**5285 Port Royal Road**
**Springfield, VA 22161**

**NOTICE OF MAILING CHANGE**

☐ Check here if you wish to discontinue receiving this publication.

☐ Check here if your address has changed and you wish to continue receiving this publication. (Be sure to furnish your complete address including zip code.)

Tear off cover with address label still affixed and send to:

Computer Support Center
ICRDB Program
IIT Research Institute
10 West 35th Street
Chicago IL. 60616

CB 17/82/05

NCI/ICRDB/CB17 82/05

PB82 931805

# ICRDB CANCERGRAM

# IMMUNOBIOLOGY AND CANCER

## Identification and Characterization of Immune Cells

SERIES CB17 No. 82/05 MAY, 1982

This Cancergram is a service of the INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM of the U.S. National Cancer Institute. Every few weeks, an updated Cancergram containing abstracts of selected cancer-related articles recently published in more than 3000 journals, and dealing with the topic indicated by the above title, is sent to researchers working in this area. These researchers are identified on the basis of the description of their current research project that has been submitted to the ICRDB Program, directly or via granting agencies.

This Cancergram is prepared by the Cancer Information Dissemination and Analysis Center (CIDAC) for Virology, Immunology, and Biology. ***If this Cancergram is useful and valuable, please send your comments to the CIDAC address below, since future editions depend on user satisfaction and user needs:***

CIDAC FOR VIROLOGY, IMMUNOLOGY, AND BIOLOGY
SCIENCE INFORMATION SERVICES
FRANKLIN INSTITUTE RESEARCH LABORATORIES
20TH AND RACE STREETS
PHILADELPHIA, PA 19103

NEWARK PUBLIC LIBRARY

MAY 17 1982

U. S. GOVT. PUBS.
DEPOSITORY 376

VIDEOTAPES ON CURRENT TOPICS IN CANCER RESEARCH ARE NOW AVAILABLE ON LOAN FROM THE ICRDB PROGRAM. SEE THE BACK PAGES OF YOUR CANCERGRAM FOR DETAILS.

*In this issue:*


- CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS..... 1-18
- DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS..... 19-36
- LYMPHOCYTE AND DIFFERENTIATION ANTIGENS..... 37-45
- CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION..... 46-53
- EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS..... 54-59
- OTHER RELATED STUDIES..... 60-69


U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service • National Institutes of Health • National Cancer Institute

HE 20.3173/2:

## CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS

### 1. CLONING OF A FUNCTIONAL GENE RESPONSIBLE FOR THE EXPRESSION OF A CELL SURFACE ANTIGEN CORRELATED WITH HUMAN CHRONIC LYMPHOCYTIC LEUKEMIA.

Stanners CP, Lam T, Chamberlain JW, Stewart SS, Price GB
Dept. Medical Biophysics, Univ. Toronto, Ontario Cancer Inst., 500 Sherbourne St., Toronto, Ontario M4X 1K9, Canada
Cell; 27(1,part2):211-221 1981

A cell-cell hybrid of a Chinese hamster ovary (CHO) cell line and human peripheral blood lymphoblasts from a patient with B-cell chronic lymphocytic leukemia produces a surface antigen dete ctable by a monoclonal antibody. This surface antigen can be detected at significant levels on a fraction of chronic lymphocytic leukemia cells, but not on normal human lymphocytes from peripheral blood or bone marrow. Two different clones capable of transforming mouse cells to produce the surface antigen were isolated from a gene library of the hybrid cell by identification of small portions of the library containing functional genes, followed by detection of clones with human-specific reiterated sequences. Both clones also contain CHO-specific reiterated sequences and are therefore human-CHO recombinants. From the frequency of antigen-producing clones in the library, we estimate that they were present in the hybrid cell genome at a copy number of 100 to 1,000. (Author abstract) (32 Refs)

### 2. IMMUNOLOGIC CHARACTERIZATION AND ULTRASTRUCTURAL CORRELATIONS FOR 125 CASES OF B- AND T-CELL LEUKEMIAS: STUDIES OF CHRONIC AND ACUTE LYMPHOCYTIC, PROLYMPHOCYTIC, LYMPHOSARCOMA CELL AND HAIRY CELL LEUKEMIA, SEZARY'S SYNDROME, AND OTHER LYMPHOID LEUKEMIAS.

Said JW, Pinkus GS
(c/o Pinkus) Dept. Pathology, Brigham and Women's Hosp., 75 Francis St., Boston, MA, 02115
Cancer; 48(12):2630-2642 1981

Peripheral blood from 125 patients (160 specimens) with various types of lymphoid leukemias was evaluated for B- and T-cell markers (E rosettes, C3 and Fc receptors, and surface immunoglobulin). B-cell leukemias comprised 82% of the series and included chronic lymphocytic leukemia (69/71 cases), acute lymphocytic leukemia (1/18 cases), lymphosarcoma cell leukemia (15/18 cases), prolymphocytic leukemia (1 case), plasma cell leukemia (1 case), hairy cell leukemia (12/12 cases), and the leukemic phase of 'histiocytic' lymphoma and Waldenstrom's macroglobulinemia (1 case each). Within the B-cell group, certain leukemias exhibited distinct patterns of lymphocyte surface markers. Three cases of lymphosarcoma cell leukemia revealed both T and B cell markers (E-rosette formation and monoclonal SIg). T-cell leukemias comprised 12% of the series and included chronic lymphocytic leukemia (2/71 cases), acute lymphocytic leukemia (11/18 cases), and Sezary's syndrome (2/2 cases). In eight cases of acute lymphocytic leukemia, the majority of the cells demonstrated no definable markers (non-B, non-T cell type). Ultrastructural studies, performed in selected cases, were correlated with immunologic findings. Distinctive morphologic features were observed for different variants of B- and T-cell leukemias. Neoplastic cells of T-cell leukemias revealed a greater nuclear irregularity than B-cell proliferations, as assessed by the nuclear contour index (ratio of circumference to the square root of the nuclear area). The cytoplasmic feature most predictive of immunologic cell type was abundant rough endoplasmic reticulum, suggesting plasmacytoid differentiation, observed in some B-cell proliferations. (Author abstract) (70 Refs)

### 3. HUMAN LYMPHOCYTE SURFACE ANTIGENS. PART 1. PRODUCTION AND CHARACTERIZATION OF HETEROANTISERA AGAINST CELL LINES DERIVED FROM T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA AND ADULT T-CELL LEUKEMIA.

Yoshimoto S
Second Dept. Internal Medicine, Okayama Univ. Medical Sch., Okayama, Japan
Nippon Ketsueki Gakkai Zasshi; 44(6):1153-1162 1981

Two heteroantisera were produced by immunizing NZW rabbits with cells of TALL-1 or MT-1. These antisera were rendered T-cell specific after absorption with human RBC acute myelogenous leukemia cells, surface Ig-positive chronic lymphocytic leukemia cells and several non-T lymphoblastoid cell lines. Absorbed antisera, anti-TALL-1 and anti-MT-1, were tested for reactivities with normal and malignant T-cells and cells of other hematological malignancies by indirect membrane immunofluorescence. Anti-TALL-1 and anti-MT-1 were uniformly reactive with normal thymocytes and peripheral blood T-lymphocytes, and their reactivities against these two populations of T-cells were almost completely abolished by absorption with normal thymocytes or peripheral blood lymphocytes (pbl). However, different reactivities were observed between these antisera. (1) Anti-TALL-1 was highly reactive with cells of T-ALL cell lines but only minimally with MT-1 and ATL cells. On the other hand, anti-MT-1 was highly reactive with MT-1 and ATL cells whereas its reactivities with cells of T-ALL cell lines were variable (10-67%). (2) Absorption of anti-TALL-1 with MT-1 cells eliminated reactivities with ATL cells but not with normal thymocytes and pbl. Similarly, absorption of anti-MT-1 with TALL-1 cells eliminated reactivities with T-ALL cell lines but not with normal thymocytes and pbl. There seems to be at least two distinct differentiation antigens in the normal T-cell series. One is recognized by anti-TALL-1 and the other by anti-MT-1. Antigens of T-ALL and ATL cells are distinct from those of normal T-cells. Antigens of ATL cells are homogeneous while those of T-ALL cells more heterogeneous and thus T-ALL may be further divided into subgroups. (44 Refs) (In JPN)

### 4. PRE-T CHRONIC LYMPHOCYTIC LEUKEMIA WITH COMMON ACUTE LYMPHOBLASTIC LEUKEMIA ANTIGEN. A NEW IMMUNOLOGIC VARIANT.

Chan JK, Stass SA, Akwari AM, Folds JD
(c/o Stass) Div. Pathology, St. Jude Children's Res. Hosp., 332 N. Lauderdale, Memphis, TN, 38101
Am J Clin Pathol; 76(6):837-840 1981

Chronic lymphocytic leukemia (CLL) is a B cell disorder but occasionally may have the characteristics of a T cell and rarely as a dual T and B cell. A case of pre-T CLL with common acute lymphoblastic leukemia antigens is presented. The Markers Studies of the bone marrow lymphocytes were +HLA, +cALL, +EAC, +Ia, -TdT, -E and peripheral blood lymphocytes were +HTLA, +Ia, -cALL, -EAC, -TdT, -E. The poor co urse of our petient suggests that more detail subtyping of CLL to identify similar subtype may provide additional prognostic information. (Author abstract) (27 Refs)

## 5. TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE IN ADULT LYMPHOBLASTIC LEUKEMIA: RELATIONSHIP WITH BLAST CELL COUNT.

Baccarani M, Marini M, Bagnara G, Gobbi M, Saviotti F, Brunelli M, Tura S
Istituto di Istologia e Embriologia Generale, via Belmeloro, 8, 40126 Bologna, Italy
Haematologica (Pavia); 66(5):579-587 1981

The relationship of blast cell count to terminal deoxynucleotidyl transferase (TDT) levels were studied. Biochemical assays were carried out on the peripheral blood cells of 27 adult patients with acute lymphoblastic leukemia (ALL) TDT activity was positive in 18/19 patients with blast cell counts greater than 0.5 x 10(3)/ul. All patients who were positive when assayed for RBC rosette formation and for surface immunoglobulins were TDT positive. A number of patients with TDT positive blast cells were studied during induction therapy or at early relapse when their blast cell counts were lower than 0.5 x 10(3)/ul. In 11/20 assays, TDT was detectable in spite of the very low blast cell number. In patients presenting with 'oligoblastic' leukemia (mean blast cell count 0.15 x 10(3)/ul), the TDT assay was always negative. The comparison of results suggested that in the oligoblastic patients, TDT negativity was not merely due to the paucity of blast cells in the sample studied, but reflected a true absence or a very low level of enzyme activity. (13 Refs)

## 6. CHRONIC LYMPHATIC LEUKEMIA OF B-CELL TYPE: CLINICAL AND MORPHOLOGICAL INVESTIGATIONS FOR DIAGNOSTIC DIFFERENTIATION.

Schwarzmeier JD, Radaszkiewicz T, Graninger W, Hofer F, Paietta E, Moser C
I. Med. Univ.-Klinik, Lazarettgasse 14, A-1090 Wien, Austria
Klin Wochenschr; 59(23):1313-1318 1981

Chronic lymphatic leukemia (CLL) was diagnosed in 71 patients based on clinical data. Most of the patients were in the stages 0, I and II; only 18% were in the stages III and IV according to Rai. In all cases, the disease was characterized by an increased number of B lymphocytes (B-CLL). The B cells mostly expressed a weak fluorescence intensity when tested for membrane bound immunoglobulins (Ig). In accordance to that, the quantitative measurement of Ig in the serum revealed a decrease of one or more Ig classes in 72% of the patients. No correlation existed between the number of B lymphocytes (and T lymphocytes) or the Ig concentration in the serum and the stage of the disease. To distinguish the CLL from related lymphoproliferative disorders, especially the immunocytic lymphoma, lymph node biopsies were examined histologically and immunomorphologically for intracytoplasmic Ig. This examination confirmed the diagnosis of CLL in 33 out of 40 cases. Six lymph nodes were classified as immunocytic lympho ma of the lymphoplasmacytoid type. In three of the latter, the immunocytic lymphoma was clinically associated with decreased Ig concentrations in the serum. These findings emphasize that the clinically established diagnosis of CLL should be corroborated by immunomorphology. (Author abstract) (26 Refs) (In GER)

## 7. SURFACE MARKERS STUDIES IN B-CELL LEUKAEMIAS WITH THE MONOCLONAL ANTIBODY FMC7 (MEETING ABSTRACT).

Catovsky D, Cherchi M, Matutes E, Brooks D, Bradley J, Zola H
Leukaemia Unit, Royal Postgraduate Medical School, London, England
Br J Haematol; 49(1):137 1981

A monoclonal antibody prepared by somatic cell hybridization against the human B-lymphoblastoid cell line HIRK, designated FMC7, has been tested by indirect immunofluorescence in 68 cases of B-cell leukemia. The following diseases were studied: B-cell chronic lymphocytic leukemia (B-CLL), B-prolymphocytic leukemia (B-PLL), B-hairy cell leukemia (B-HCL), and B-cell lymphomas in leukemic phase. Four of the 56 cases of B-CLL which were FMC7 positive had morphological features suggestive of 'prolymphocytoid' (PL) transformation and three of them (two with PL change) had also bright SmIg staining. The probability of FMC7 being positive in B-CLL with either of those atypical features was significantly greater than in the rest. The two patients with high density of SmIg and features of PL change, but with a high percentage of mouse-RBC rosettes, appear to represent an intermediate form between B-CLL and B-PLL, hitherto unrecognized. There was an overall correlation between the intensity of immunofluorescence reaction with FMC7 and SmIg on the leukemic B-cells. However, FMC7 did not relate to any specific class of Ig and was negative in almost all B-CLL which had a weak expression of SmIg. This study demonstrates that this new monoclonal antibody may contribute to the cell characterization and classification of B-cell malignancies. (no Refs)

## 8. PATHOLOGY OF T-PRECURSOR CELLS ACUTE LYMPHOBLASTIC LEUKEMIA - WITH SPECIAL REFERENCE TO SURFACE MARKERS.

Kawashima K, Kato Y, Ogura M, Suzuki H, Watanabe E, Takamatsu J, Minami S, Isobe K, Nagura E, Yamada K, Iwamura H, Yamamura M, Yokomaku S
First Dept. Internal Medicine, Nagoya Univ. Sch. Medicine, Nagoya, Japan
Rinsho Ketsueki; 22(7):1102-1108 1981

Characteristics of cell-surface markers on leukemia cells were determined in six patients (5 men, 1 woman; 6-28 yr old) with T-precursor cell acute lymphoblastic leukemia (ALL). The patients were administered various regimens of chemotherapy that included the following drugs: daunomycin, vincristine, prednisolone, endoxan, 6-mercaptopurine, cyclophosphamide, and procarbazine. Complete remission was induced in a short time in 5/6 patients, but the duration of remission was short (1-8.5 mo). CNS leukemia or hematological relapse occurred during relapse, and 5/6 patients died within 2 yr of treatment. The leukemia cells from the patients lacked surface immunoglobulin and receptors for mouse RBC but had receptors for complement (C3) and untreated sheep RBCs. High terminal deoxynucleotidyl transferase (TdT) activity was observed peripheral blood and bone marrow cells in 4/5 patients. Anterior mediastinal tumors were discovered at autopsy in two patients; dominant cells in these two patients were C3+. Because of similarities in cell surface markers, the T-precursor leukemia cells from the patients with ALL and early fetal thymocytes were thought to resemble each other in T-cell maturation. (28 Refs) (In JPN)

## 9. DEFECTIVE IMMUNOREGULATORY T-CELL FUNCTION IN CHRONIC LYMPHOCYTIC LEUKEMIA.

Han T, Ozer H, Henderson ES, Dadey F, Nussbaum-Blumenson A, Barcos M
Medical Oncology, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Blood; 58(6):1182-1189 1981

Chronic lymphocytic leukemia (CLL) of B-cell origin results in the malignant proliferation of small Ig-bearing lymphocytes. There is currently a controversy in the literature regarding both the ability of this leukemic population to differentiate into mature plasma cells, as well as the ability of apparently normal

T cells from these patients to regulate allogeneic B-cell differentiation. In the present study we have examined the lymphocytes of CLL patients in various clinical stages of their disease and with different surface phenotypes of their leukemic B-cell population. Our results show that leukemic CLL B cells from all 20 patients (including 1 patient with a monoclonal IgM paraprotein and another with a monoclonal IgG paraprotein) are incapable of further differentiation even in the absence of suppressor T cells and the presence of helper T lymphocytes. This lack of capacity to differentiate is unaffected by clinical stage, by therapy, or by the phenotype of the malignant population. Since the leukemic B population did not suppress normal allogeneic B-cell differentiation, the maturation deficit is evidently intrinsic to the leukemic clone rather than a result of activity of non-T suppressor cells. T helper function was also variably depressed in the blood of some patients with CLL, and this depression did not correlate with clinical stage, with therapy, or with the degree of lymphocytosis. Dysfunction of radiosensitive T suppressor cells was found to be the most consistent regulatory deficit of CLL T cells. Each of 11 patients whose leukemic cell population was of the mu delta, mu alpha, or mu phenotype had both helper and suppressor cell defects. In contrast, three patients with gamma-bearing leukemic populations exhibited normal T helper as well as normal radiosensitive suppressor T-cell function. These results emphasize the heterogeneity of immunoregulatory T-cell function in patients with CLL and may indicate immunologically unique subgroups of patients with this malignancy. (Author abstract) (18 Refs)

## 10. DIFFERENTIATION OF CHRONIC LYMPHOCYTIC LEUKEMIA FROM HODGKIN'S DISEASE USING IMMUNOLOGIC MARKER STUDIES.

**Colby TV, Warnke RA, Burke JS, Dorfman RF**
**Dept. Pathology, Stanford Univ. Medical Center, Stanford, CA, 94305**
**Am J Surg Pathol; 5(7):707-710 1981**

Use of immunofluorescence technics for differentiation of chronic lymphocytic leukemia (CLL) from Hodgkin's disease (HD) in a 64-yr-old man is reported. Repeated lymph node biopsies showed typical lymphocyte-predominant HD, but leukocytosis and the pattern of bone marrow infiltration were indicative of CLL. Indirect immunofluorescence with F(ab')2 antibody fragments showed a monoclonal light-chain pattern. These findings confirmed the diagnosis of CLL. (7 Refs)

## 11. ADENOSINE DEAMINASE AND ECTO-5'-NUCLEOTIDASE ACTIVITIES IN VARIOUS LEUKEMIAS WITH SPECIAL REFERENCE TO BLAST CRISIS: SIGNIFICANCE OF ECTO-5'-NUCLEOTIDASE IN LYMPHOID BLAST CRISIS OF CHRONIC MYELOID LEUKEMIA.

**Koya M, Kanoh T, Sawada H, Uchino H, Ueda K**
**First Div., Dept. Internal Medicine, Faculty Medicine, Kyoto Univ., Sakyo-ku, Kyoto 606, Japan**
**Blood; 58(6):1107-1111 1981**

Adenosine deaminase (ADA) and ecto-5'-nucleotidase (5'-N) activities were examined in peripheral leukocytes from patients with leukemias, including nine patients with chronic myeloid leukemia (CML) in blast crisis. Four of nine cases of CML in blast crisis were myeloid and the remaining lymphoid morphologically. The diagnosis of CML in lymphoid blast crisis was further contributed by the measurement of terminal deoxynucleotidyl transferase (TdT) activity. In all four cases of lymphoid blast crisis and one of myeloid blast crisis, leukemia cells had high 5'-N activity, while there was little or no detectable activity in those from four cases of myeloid blast crisis and all of CML in chronic phase. ADA activity was high in seven of nine patients with blast crisis. Taken together, leukemia cells from two cases of lymphoid blast crisis had high ADA and 5'-N activities comparable to those in acute lymphocytic leukemia (ALL) cells. In contrast, the enzyme activities of leukemia cells from all but one patient in myeloid blast crisis were in a range similar to acute myeloid leukemia cells. The implications of these findings are as follows: (1) 5'-N may be used as a new biochemical marker of CML in lymphoid blast crisis. (2) Some lymphoid cells of CML in blast crisis have high ADA, 5'-N, and TdT activities and thus are very similar to ALL cells. (Author abstract) (38 Refs)

## 12. HIGH LEVELS OF 5'-NUCLEOTIDASE ACTIVITY IN BLASTIC CHRONIC MYELOGENOUS LEUKEMIA WITH COMMON ALL-ANTIGEN.

**Gutensohn W, Thiel E**
**Arbeitsgruppe Biochemische Humangenetik, Institut fur Anthropologie und Humangen etik, Schillerstrasse 42, D 8000 Munich 2, W. Germany**
**Leuk Res; 5(6):505-510 1981**

Levels of 5'nucleotidase (5'-N) on surfaces of leukemia cells were determined for 44 patients in lymphoid blast crisis (LY-BC) of chronic myelogenous leukemia (CML) with or without common acute lymphoblastic leukemia (cALL) antigen (cALLA) and for 52 patients with acute myeloblastic (AML) or acute lymphoblastic (ALL) leukemia. The 5'-N activities of mononuclear cell preparations from 50 healthy blood donors ranged from 1.2 to 14.5 nanomoles AMP hydrolyzed/hr/10(6) cells; this activity was mainly due to T and B lymphocytes. In 12 cases of cALL, blast cells derived from blood and bone marrow of the same patient were compared; no difference in immunological phenotype expression was noted, and the 5'-N activity was the same in both cell sources. Cells from the AML patients, diagnosed mainly on the basis of hematological criteria, were cALLA-negative. Diagnosis of the cALL patients was based on the absence of B or T markers and the expression of cALLA. The difference in 5'-N activities of AML and cALL cells and the difference in 5'-N activities of myeloid blast crisis (MY-BC) and LY-BC cells were both statistically significant. A wide overlap in 5'-N activities for AML and cALL limits the usefulness of the 5'-N determination. No overlap of 5'-N activity was observed, however, for the LY-BC and MY-BC cells. The LY-BC cells of CML characterized by cALLA had high 5'-N levels, while cALLA-negative blast crisis was correlated with a decreasc in 5'-N activity. The results indicated that 5'-N affords an additional, easily-testable biochemical marker that may have diagnostic and prognostic value in blastic CML. (31 Refs)

## 13. ADVANCED CUTANEOUS T CELL LYMPHOMA (TUMEURS D'EMBLEE TYPE): THE DIFFERENTIAL CAPACITY OF E CELL ROSETTING, NON SPECIFIC ESTERASE STAINING AND ANTI-HTLA PEROXIDASE METHODS FOR CYTOLOGICAL DIAGNOSIS (MEETING ABSTRACT).

**Holden CA, Staughton RC, MacDonald DM**
**Department of Dermatology, Guy's Hospital, London, England**
**Br J Dermatol; 105(3):346 1981**

The diagnosis of cutaneous T cell lymphoma depends on cytological typing but T lymphocyte markers are sequentially lost during in vitro transformation. Sections from the cutaneous nodules of a 71-yr-old male with tumeurs d'emblee type cutaneous T cell lymphoma were examined by three common-

ly used methods for T lymphocyte identification. (1) Collagenase incubated skin was mechanically disintegrated to release viable cells. The proportion of cells retaining the ability to rosette sheep RBC was estimated. (2) Cryostat sections of prefixed frozen tissue were stained for the presence of acid-alpha-naphthyl acetate esterase (ANAE) activity. (3) Tissue sections were incubated with anti-human thymus lymphocytic antigen (HTLA) serum and peroxidase conjugate, and examined by light and electron microscopy to revea l the proportion of cells retaining the HTLA membrane antigen. Six percent of the extracted cells were capable of E rosetting. ANAE activity of T pattern was present in only occasional cells. The immunoperoxidase technique demonstrated characteristic positive labelling of the majority of infiltrating cells. Ultrastructural examination confirmed the presence of HTLA membrane antigen on the cell membrane. The results demonstrate, in vivo, the persistence of HTLA membrane antigen in cutaneous lymphoma T cells which have lost their ability for E rosetting and their ANAE activity. They support the in vitro findings of sequential loss of cell characteristics and suggest that the demonstration of HTLA may identify T lymphocytes which could otherwise be considered as null cells. (no Refs)

## 14. IMMUNOCOMPETENCE AND MALIGNANT LYMPHOMA: IMMUNOLOGIC STATUS BEFORE THERAPY.

**Anderson TC, Jones SE, Soehnlen BJ, Moon TE, Griffith K, Stanley P**

**Section Hematology Oncology, Dept. Internal Medicine, Univ. Arizona Coll. Medicine, Tucson, Arizona, 85724**

**Cancer; 48(12):2702-2709 1981**

One-hundred-eighty-six previously untreated patients with malignant lymphoma were evaluated for immunocompetence by means of several tests of immune function: total circulating lymphocytes, T cells (E-rosettes), B cells (EAC-rosettes), delayed hypersensitivity to six recall antigens, serum immunoglobulins, mixed lymphocyte culture, and lymphocyte mitogenic response to phytohemagglutinin and pokeweed mitogen. The results were correlated with histology, stage, and clinical features. Diffuse lymphomas, especially diffuse histiocytic (large cell) (DHL), were associated with decreased absolute lymphocytes and E-rosette forming cells. Skin test reactivity varied with both histology and stage. For example, only one of six tests was impaired in diffuse lymphocytic well differentiated (DLWD) lymphoma in contrast to two of six in localized DHL and five of six in advanced DHL. Patients with nodular lymphoma exhibited depressed mean levels of IgA and IgG, while only IgA was significantly decreased in diffuse lymphoma. Mitogen stimulation was depressed in all groups, although mixed lymphocyte cultures did not differ significantly from controls. In summary, there is a spectrum of immunodeficiency of both B and T cell type in patients with malignant lymphoma that correlates with histology and stage. Implications and possible mechanisms of these observations are discussed. (Author abstract) (25 Refs)

## 15. THE PATHOPHYSIOLOGY OF MALIGNANT LYMPHOMA FROM THE HEMATOLOGICAL POINT OF VIEW: (1) THE LEUKEMIC TRANSFORMATION OF MALIGNANT LYMPHOMA, ESPECIALLY TRADITIONAL 'RETICULUM CELL SARCOMA'.

**Kinoshita K, Amagasaki T, Yamada Y, Kamihira S, Muta T, Kitamura T, Ikeda S**

**Dept. Hematology, Atomic Disease Inst., Nagasaki Univ. Sch. Medicine, Nagasaki, Japan**

**Nippon Ketsueki Gakkai Zasshi; 44(6):1169-1177 1981**

The size of leukemic cells in 15 cases of traditional 'reticulum cell sarcoma' with leukemic manifestation was measured. Almost all cases were of T-cell origin in nature on the basis of spontaneous rosette formation with sheep erythrocytes (E-rosettes) and cell morphology. As the result, they were divided into the small cell dominant group (8 cases) and the large cell dominant group (7 cases), respectively. In the former more than 80% of the leukemic cells in the peripheral blood were less than 12 u in cell diameter and in the latter more than 50% of the leukemic cells were larger than 15 u in size. In the small cell dominant group, the majority of the peripheral leukemic cells showed the obvious lymphocytic differentiation with condensed nuclear chromatin and scant cytoplasm, although in many of the cases lymphomatous infiltrate was characterized by large or pleomorphic lymphoid cells, accompanied by the proliferation of post capillary venule-like vessels (PCV) and transmural migration of small abnormal lymphoid cells. The clinicohematological features were similar to those of so-called 'Adult T-cell leukemia' in Japan. On the other hand, the large cell dominant group showed the histology of monotonous infiltrate of large lymphoid cells without the proliferation of PCV and transmural migration of the lymphoid cells. Hematological examination revealed that the leukemic cells were large blastic cells with basophilic cytoplasm and they did not increase to such a degree that WBC count was markedly elevated. The clinical features were lymphomatous presentation with massive lymphadenopathy. The mechanism of leukemic manifestation is also discussed. (Author abstract) (30 Refs) (In JPN)

## 16. NODULAR MIXED CELL LYMPHOMA WITH MONOCLONAL GAMMOPATHY.

**Bain GO, Belch A**

**Cross Cancer Inst., 11560 University Ave., Edmonton, Alberta T6G 1Z2, Canada**

**Am J Clin Pathol; 76(6):832-837 1981**

Malignant lymphomas are rarely accompanied by a serum M component. Such neoplasms are usually of lymphocytic cell type and, with extremely rare exceptions, of diffuse pattern. A patient with an unusual malignant lymphoma of mixed cell type characterized by follicular structures and vascular proliferation was found to have a serum monoclonal gammopathy (IgM kappa) of over 4 g/dl. Remission accompanied by a pronounced reduction in the M protein was achieved with Chlorambucil. Subsequent relapse was characterized by the emergence of a large cell lymphoma with IgM kappa surface immunoglobulin. No concomitant rise in the serum M component accompanied relapse. (Author abstract) (18 Refs)

### 17. COEXISTENCE OF A PRIMARY IMMUNODEFICIENCY DISORDER AND HODGKIN'S DISEASE: EVIDENCE AGAINST A B-LYMPHOCYTE ORIGIN FOR THE REED-STERNBERG CELL.

Bobrove AM, Onder O, Myers TJ, Rickles FR, Pastuszak WT, Martin RS, Hild DH
Palo Alto Medical Clinic, 300 Homer Ave., Palo Alto, CA, 94301
Cancer; 48(12):2624-2629 1981

A 44-yr-old woman with a life-long history of recurrent sinopulmonary infections developed Hodgkin's disease with characteristic Reed-Sternberg cells in a biopsy specimen of a mediastinal lymph node. Hypogammaglobulinemia was documented on several serum determinations and plasma cells were absent from biopsy specimens of the lymph node and bone marrow. Immunochemical studies failed to demonstrate any B lymphocytes bearing surface immunoglobulin or Fc-receptors for IgG in the peripheral blood. Pokeweed mitogen stimulation of the patient's peripheral blood lymphocytes in vitro resulted in the development of virtually no plasma cells. Peripheral blood T-lymphocyte number and function were defective initially. Following chemotherapy and radiotherapy, peripheral blood E-rosette-forming cells returned to normal, but T-cell function remained defective and B lymphocytes remained undetectable. These findings are compatible with the presence of two separate immune disorders: a primary hypogammaglobulinemia and Hodgkin's disease. The absence of lymphocytes bearing surface Ig or Fc-receptors for IgG in this patient adds further support against a B-lymphocyte origin for the Reed-Sternberg cell. (Author abstract) (32 Refs)

### 18. DETECTION OF TERMINAL TRANSFERASE IN PARAFFIN SECTIONS WITH THE IMMUNOPEROXIDASE TECHNIQUE.

Halverson CA, Falini B, Taylor CR, Parker JW
Dept. Pathology, Univ. Southern California Sch. Medicine, Los Angeles, CA
Am J Pathol; 105(3):241-254 1981

Terminal deoxynucleotidyl transferase (TdT) is an early T-cell differentiation marker in a number of species, including man. We have demonstrated TdT in the nuclei of cortical thymocytes in paraffin-embedded sections of calf, rat, and human thymus by indirect immunoperoxidase techniques. In addition, these techniques have been used to verify and extend enzyme assay results by detecting TdT in blast cells from 10 patients with convoluted T-cell lymphoma/leukemia, 1 patient with acute granulocytic leukemia, 1 patient with chronic granulocytic leukemia in blast crisis, and 1 patient with non-T non-B acute lymphocytic leukemia. (Author abstract) (49 Refs)

## DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS

### 19. THE USE OF MODIFIED CUNNINGHAM CHAMBERS FOR THE ENUMERATION OF H ROSETTES, E ROSETTES, AND LYMPHOCYTE-TUMOR CELL CONJUGATES.

Pross HF, Gallinger LA, Rubin P, Baines MG
Ontario Cancer Foundation, Kingston Clinic, King Street West, Kingston, Ontario K2L 2V7, Canada
Int Arch Allergy Appl Immunol; 66(4):365-371 1981

In this paper, we have described the use of a slide-coverslip Cunningham chamber which is ideal for counting delicate rosettes and lymphocyte-tumor cell conjugates. The ease of construction , facility of use, and economy of cost in comparison with hemocytometers make the use of these chambers the method of choice for rosette counts in general. In contrast to standard double-slide Cunningham chambers, the design of these rosette chambers is such that they can be used with ordinary light microscope objectives (including oil immersion), they can be more easily loaded without trapping air bubbles, and they can be sealed without tilting the slide. As an example of one potential application of these chambers to tumor immunology, data have been presented showing the high proportion of lymphocyte-tumor cell conjugates which can be formed by human peripheral blood cells. The ability of any particular tumor cell to form conjugates did not necessarily reflect the susceptibility of that cell type to natural killer (NK) cell-mediated lysis, nor was there any evidence that E rosette-forming cells preferentially formed conjugate in comparison to non E rosette-forming cells. (Author abstract) (12 Refs)

### 20. ROLE OF BETA1H FOR THE BINDING OF C3B-COATED PARTICLES TO HUMAN LYMPHOID AND PHAGOCYTIC CELLS.

Schmitt M, Mussel HH, Hammann KP, Scheiner O, Dierich MP
(c/o Dierich), Institut fur Medizinische Mikrobiologie, Obere Zahlbacher Strasse 67, D-6500 Mainz, W. Germany
Eur J Immunol; 11(10):739-745 1981

Coating of EAC14oxy23b with highly purified human serum beta1H globulin (beta1H) led to acceleration of rosette formation with human peripheral blood lymphocytes (PBL), tonsil lymphocytes, B lymphoblastoid (Raji) cells, granulocytes and monocytes. This reaction was discernible from C36-dependent rosette formation. Enhancement of rosette formation of C3b cells by beta1H was most effective at limiting amounts of C3 per EAC14oxy23b. The beta1H effect was not due to trace contamination with C3b inactivator. Beta1H-dependent rosette formation with the various lymphoid and phagocytic cells could be suppressed by the F(ab')2 fragment of anti-beta1H suggesting beta1H-mediated binding of beta1H-coated particles to complement receptor-positive (CR+) cells. In turn, binding of fluid-phase beta1H to lymphoid and phagocytic cells could be demonstrated by fluorescence and by 14C-labeled beta1H. In addition, the functional status of these cells with respect to their receptor reactivity was altered. Treatment of normal lymphocytes (PBL, tonsil lymphocytes) and of granulocytes with beta1H improved their rosette formation with both EAC14oxy23b and EAC14oxy23b-beta1H. The reaction of monocytes was hardly affected. The beta1H effect on Raji cells resulted in reduced rosette formation with EAC14oxy23b-beta1H, while binding of EAC14oxy23b remained unchanged. These results suggest the presence of sites on CR+ cells, to which soluble and particle-bound beta1H can bind, leading to alteration of the functional status of the cells. In all likelihood, EAC14oxy23b can attach to the beta1H-binding sites on CR+ cells. (Author abstract) (28 Refs)

### 21. HIGH AFFINITY BINDING OF 125I-LABELED MOUSE INTERFERON TO A SPECIFIC CELL SURFACE RECEPTOR. II. ANALYSIS OF BINDING PROPERTIES.

Aguet M, Blanchard B
Institut fur Immunologie und Virologie der Universitat Zurich, Gloriastrasse 32 B, Postfach, CH-8028 Zurich, Switzerland
Virology; 115(2):249-261 1981

Direct ligand-binding studies with highly purified 125I-labeled virus-induced mouse interferon on mouse lymphoma

L1210 cells revealed a direct correlation of specific high-affinity binding with the biologic response to interferon. Neutralization of the antiviral effect by anti-interferon gamma globulin occurred at the same antibody concentration as the inhibition of specific binding. These results suggest that specific high-affinity binding of 125I-interferon occurred at a biologically functional interferon receptor. Competitive inhibition experiments using 125I- and 127I-labeled interferon provided strong evidence that the fraction of 125I-interferon inactivated upon labeling did not bind specifically. Scatchard analysis of the binding data yielded linear plots and thus suggested that interferon binds to homogeneous noncooperative receptor sites. In contrast to a characteristic property of several peptide hormone systems, binding of 125I-interferon to its specific receptor did not induce subsequent ligand degradation. At 37 C bound interferon was rapidly released in a biologically active form without evidence for molecular degradation. The expression of interferon receptors was not modified by treatment with interferon. Trypsin treatment of target cells and inhibition of protein synthesis abolished the specific binding of 125I-interferon. three major mol wt species of Newcastle disease virus-induced mouse C 243 cell interferon were isolated separately and identified as mouse alpha and beta interferons. These interferons were shown to inhibit competitively the specific binding of the highly purified labeled starting material which contained all three size species, thus providing evidence for a common receptor site for mouse alpha and beta interferon. (Author abstract) (24 Refs)

## 22. VASOACTIVE INTESTINAL POLYPEPTIDE MODULATION OF LYMPHOCYTE ADENYLATE CYCLASE.

**O'Dorisio MS, Hermina NS, O'Dorisio TM, Balcerzak SP**
**Dept. Medicine, Ohio State Univ., 410 W. 10th Ave., Columbus, OH, 43210**
**J Immunol; 127(6):2551-2554 1981**

Vasoactive intestinal polypeptide (VIP) was found to be a potent stimulator of lymphocyte adenylate cyclase activity. VIP-induced activation of adenylate cyclase was specific for lymphocytes among peripheral blood cells; ie, VIP did not stimulate the adenylate cyclase activity of neutrophils, monocytes, or platelets. The VIP-induced activation of lymphocyte adenylate cyclase was time, temperature, an d concentration dependent. VIP and the GTP analog, Gpp(NH)p, acted synergistically to stimulate lymphocyte adenylate cyclase; stimulation by VIP and PGE1 was additive; and VIP activation was antagonized by somatostatin. VIP-mediated activation of lymphocyte adenylate cyclase was observed in normal human T cells, B cells obtained from a patient with chronic lymphocytic leukemia, and a human T cell culture line. The Raji human B cell culture line did possess adenylate cyclase activity, but this activity was not stimulated by VIP. These results suggest that lymphocytes possess functional receptors for VIP and that this peptide may play a role in modulation of lymphocyte function. (Author abstract) (41 Refs)

## 23. BINDING OF C-REACTIVE PROTEIN TO HUMAN LYMPHOCYTES: II. INTERACTION WITH A SUBSET OF CELLS BEARING THE FC RECEPTOR.

**James K, Hansen B, Gewurz H**
**Dept. Immunology/Microbiology, Rush Medical Coll., Chicago, IL, 60612**
**J Immunol; 127(6):2545-2550 1981**

In the preceding paper we reported that C-reactive protein (CRP) in the presence of a multimeric binding specificity such as C-polysaccharide (CPS) binds to a small percentage of peripheral blood lymphocytes (PBL). In the present paper additional methods for demonstrating this binding were developed and utilized to help characterize the CRP-binding cell. Heat-modified CRP and E-CPS-CRP each were found to bind to a similar percentage of PBL by microscopic visualization, and an identical degree of binding was observed by cytofluorimetric analysis. Multiple marker studies indicated that CRP-binding cells are found in the T cell, B cell, and null cell categories in a ratio of 2:1:1, respectively. Preferential overlap was seen with IgG FcR-bearing cells, which accounted for 70% of the CRP-binding cells; however, only 12% of the FcR cells bound CRP. These studies indicate that CRP-binding cells predominantly represent a subset of cells bearing FcR, and these cells have the morphologic characteristics of large granular lymphocytes. CRP in the presence of CPS bound to cells of multiple human and murine cultured lines shown to have IgG FcR reactivity, but showed lesser or no binding to cell lines negative for FcR. The precise morphologic and functional characterization of the CRP-binding cells and the nature of the binding site are yet to be established. (Author abstract) (49 Refs)

## 24. NONSPECIFIC IMMUNOSUPPRESSIVE FACTORS IN MALIGNANT ASCITES: FURTHER CHARACTERIZATION AND POSSIBLE RELATIONSHIP TO ERYTHROCYTE RECEPTORS OF HUMAN PERIPHERAL T CELLS.

**Oh SK, Moolten FL**
**Dept. Microbiology, Boston Univ. Sch. Medicine, Boston, MA, 02118**
**J Immunol; 127(6):2300-2307 1981**

Nonspecific suppressor factor has been purified from malignant human ascites through partial delipidation, ammonium sulfate precipitation, ACA-22 gel filtration followed by goat anti-huma n IgG immunoadsorbent chromatography. Mol wt estimated by SDS-PAGE under mild reducing conditions is 50,000 and 25,000 under vigorous reducing conditions. It inhibits PHA, Con A, and PWM responses of peripheral lymphocytes by 50% at microgram concentrations per milliliter in vitro and inhibits plaque-forming cell response to SRBC at 100 ug/mouse in vivo. It also inhibits two-way mixed lymphocyte reactions and natural killer cell activities. It inhibits SRBC rosette formation of peripheral T cells and appears to be an erythrocyte receptor of peripheral T cells. (Author abstract) (56 Refs)

## 25. CELL-MEDIATED IMMUNITY TO HERPES SIMPLEX VIRUS: RECOGNITION OF TYPE-SPECIFIC AND TYPE-COMMON SURFACE ANTIGENS BY CYTOTOXIC T CELL POPULATIONS.

**Eberle R, Russell RG, Rouse BT**
**Dept. Microbiology, Coll. Liberal Arts, Univ. Tennessee, Knoxville, TN, 37916**
**Infect Immun; 34(3):795-803 1981**

In this communication, we examine the specificity of anti-herpes simplex virus (HSV) cytotoxic T lymphocytes (CTL). Serological studies of the two related HSV serotypes (HSV-1 and HSV-2) have revealed both type-specific and cross-reactive antigenic determinants in the viral envelope and on the surface of infected cells. By analysis of cytotoxicity of CTL generated in vitro by restimulation of splenocytes from mice primed with one or the other HSV serotype, the recognition of both type-specific and cross-reactive determinants on infected target cells by anti-HSV CTL was detectable. Thus, effector cells generated by priming and restimulating with the same virus recognized both type-specific and cross-reactive determi-

nants on target cells infected with the homologous virus, but only cross-reactive determinants on target cells infected with the heterologous HSV serotype. CTL generated by restimulation with the heterologous virus were capable of recognizing only the cross-reactive determinants on either HSV-1-or HSV-2-infected target cells. These results indicate that two subpopulations of CTL exist in a population of anti-HSV immune spleen cells - those which recognize type-specific determinants and those specific for cross-reactive antigenic determinants present on the surface of HSV infected cells. The type-specific subset of anti-HSV CTL was shown to recognize the gC glycoprotein of HSV-1 infected target cells. In addition to the gC glycoprotein, at least one other type-specific surface antigen was also recognized by anti-HSV CTL in addition to the cross-reactive determinants recognized by anti-HSV CTL. (Author abstract) (23 Refs)

## 26. THE SPECIFICITY OF RAT NATURAL KILLER CELLS AND CYTOTOXIC MACROPHAGES ON SOLID TUMOR-DERIVED TARGET CELLS AND SELECTED VARIANTS.

**Brooks CG, Wayner EA, Webb PJ, Gray JD, Kenwrick S, Baldwin RW**
**Program in Basic Immunology, Fred Hutchinson Cancer Center, 1124 Columbia St., S eattle, WA, 98104**
**J Immunol; 127(6):2477-2483 1981**

The specificity of rat splenic natural killer (NK) cells and BCG-activated peritoneal cytotoxic macrophages (CMphi) was evaluated. We found that NK cells and CMphi had almost identical specificity. Extensive analysis of the specificity of NK cells showed that tumor lines induced at the same site with the same carcinogen or arising spontaneously in the same tissue could have markedly different NK sensitivities. Cloning experiments revealed that tumor lines were composed of populations of cells with markedly different NK sensitivity, and that variants with altered NK sensitivity could arise spontaneously in cloned lines within a period of mo. Normal fibroblasts were relatively resistant to NK cells, but competition experiments showed that fibroblasts bound NK cells better than did most tumor cell lines. There was a significant correlation between NK sensitivity and susceptibility to hypotonic lysis. In addition, there was also a correlation between NK susceptibility and competitive activity. Cross-competition experiments indicated that there were quantitative rather than qualitative variations in NK cell-binding structures. These studies indicate that three target cell factors determine the specificity of NK cell lysis in solid tumor systems: (1) the amount of NK cell-binding structure expressed on the target cell; (2) a second factor varying between tumor lines, but not between variants of the same line, which seems to be required before cytolysis can be initiated; and (3) the osmotic fragility of the target cell, presumably related to membrane structure or the ability to repair membrane damage. (28 Refs)

## 27. ACCESSORY CELLS IN THE IN VITRO GENERATION OF TYPE C VIRUS-SPECIFIC T KILLER LYMPHOCYTES: II. DEMONSTRATION OF A T HELPER CELL IN THE SPLEEN OF IN VIVO PRIMED MICE.

**Gomard E, Wybier-Franqui J, Simmler MC, McKenzie IF, Levy JP**
**Laboratoire Immunologie et Virologie des Tumeurs, INSERM U 152, ERA 781, Hopital Cochin 27, rue du Faubourg Saint Jacques, 75645 Paris Cedex 14, France**
**J Immunol; 127(6):2291-2295 1981**

The existence of a helper T cell cooperating with cytolytic T lymphocytes (CTL) in cell-mediated anti-tumor responses specific for the virus-induced FMR antigens can be demonstrated by using unprimed thymocytes as CTL precursors and in vivo primed irradiated spleen cells as helper. The helper T cells express Thy-1.2 and Lyt-1.2 antigens at their surface, but not Lyt-2.2. The helper function required the presence of macrophages to be detected, is antigen specific, and appears unusually radiosensitive compared with previously described helper T cell function. (Author abstract) (27 Refs)

## 28. IMMUNE STATUS OF GASTROINTESTINAL (G-I) TRACT CANCER PATIENTS: CHANGES IN IGG-FC RECEPTOR-POSITIVE T-CELL VALUES BEFORE AND AFTER SURGICAL TREATMENT.

**Yasui E**
**First Dept. Surgery, Nihon Univ., Sch. Medicine, Itabashi-ku, Tokyo 173, Japan**
**Nichidai Igaku Zasshi; 40(6):591-601 1981**

The IgG-Fc receptor-positive T-cell values (T-gamma) in the peripheral blood of 50 normal individuals or benign patients (control subjects) and 111 G-I tract cancer patients (esophagus 10, stomach 59, colorectum 26, and liver, bile ducts and pancreas 16) were determined. The mean value of Tgamma in the control subjects was 6.2 +-4.2% (mean +-2 standard deviation). Therefore, in this study, patients whose Tgamma exceeded 11% were considered positive. Seventy (63%) of the 111 patients were Tgamma positive. Tgamma showed no statistically significant difference among the patients with different kinds of cancer, but it tended to increase with the extent of cancer. Tgamma showed negative correlations with the phytohemagglutinin (PHA) and concanavalin A responses and the PHA skin test. Postoperatively, Tgamma tended to decrease after major reduction of the tumor load. However, it increased with tumor regrowth and recurrence. In gastric cancer patients, excluding some who had curative or no resection of the tumor, splenectomy (either combined or solitary) had no significant effect on Tgamma. (Author abstract) (26 Refs) (In JPN)

## 29. IMMUNOHISTOCHEMISTRY OF WARTHIN'S TUMOR (MEETING ABSTRACT).

**Lee V, Tubbs R, Sheibani K, Weiss R, Sebek B, Valenzuela R**
**Division of Laboratory Medicine, Cleveland Clinic Foundation, Cleveland, OH, 44106**
**Am J Clin Pathol; 76(3):353 1981**

Several tumors are characterized by a prominent lymphocytic component. Among the more interesting of such neoplasms is the Warthin's tumor. The lymphocytic infiltrate has been variously classified as a cellular response to an epithelial neoplasm or residual lymph node involved by a purely epithelial proliferation. Three typical Warthin's tumors were studied with immunohistochemistry for surface immunoglobulins. A polyclonal light chain immunohistochemical staining distribution was observed in all three cases with prominent follicular center cell staining and apparent extracellular pooling within follicular centers. These patterns are identical to those observed in follicular hyperplasia. Also, a cell suspension was prepared from one case for surface markers evaluation. Thirty percent of the cells formed spontaneous E rosettes and 40% of the cells demonstrated polyclonal surface immunoglobulins. These observations tend to support the concept that the lymphoid cell population in Warthin's tumors represents a reactive cellular infiltrate. However, specific cellular or humoral immune responses to components of salivary glandular or ductular epithelium have not yet been identified. (no Refs)

## 30. HUMORAL AND CELLULAR NON-SPECIFIC IMMUNE RESPONSE IN UNTREATED HODGKIN- AND CERVICAL CARCINOMA PATIENTS (MEETING ABSTRACT).

**Schneiberg K, Rytwinski K**
**Department of Clinical Investigation and Haematology, Institute of Oncology, Gliwice, Poland**
**UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.**

In 58 patients with grade I-IV Hodgkin's disease, histologic type LP, NS, MC or LD and in 50 patients ill of cervical carcinoma grade II the blood levels of IgA, IgM and IgG, the immunelectrophoretic pattern of serum proteins, the absolute lymphocyte count, the per cent proportion of lymphocytes B (surface immunofluorescence) and T (SE-rosettes), the degree of blastic transformation (with phytohemagglutinin) and the activity of LT-factor(lymphotoxin - method of Spofford et al) were determined. Moreover, in Hodgkin patients the skin test with dinitrochlorobenzene (method of Catalona et al) was performed. In all patients the levels of IgA, IgM and IgG were increased. Also the appearance of increased orosomucoid, ceruloplasmin, transferrin, or haptoglobins, sometimes of paraproteins could be observed. The percentage of B lymphocytes was in Ccu patients higher than in controls, on the contrary it was lower in Hodgkin patients. In both diseases the percentage of T lymphocytes was lowered with a simultaneous relative increase in the production of the LT-factor. The degree of blastic transformation falls down in all patients. With help of the Mantel-Henszel's test for survivorship data a positive correlation between the LT-activity before treatment and prognosis was established in Ccu patients. In the group of Hodgkin patients which was less homogenous as far as sex age and clinical stage are concerned, such a correlation could not be confirmed. (no Refs)

## 31. CELL-MEDIATED IMMUNITY IN EARLY PREGNANCY AND TROPHOBLASTIC NEOPLASIA (MEETING ABSTRACT).

**Oh WS, Song SK, Cho BC, Kim SJ**
**Departments of Obstetrics and Gynaecology, Catholic Medical College, Seoul, Korea**
**Obstetrics and Gynaecology: 8th Asian Congress, October 25-31, 1981, Melbourne, Australia. Asia and Oceania Federation of Obstetricians and Gynaecologists 352 pp., 1981.**

Cell-mediated immunity studies were carried out serially in 20 healthy women, 27 healthy pregnant women and 134 patients with gestational trophoblastic neoplasia (GTN). The authors employed a battery of lymphocyte monitoring techniques: absolute lymphocyte counts, dinitrochlorobenzene (DNCB) skin testings, phytohemagglutinin (PHA) induced lymphocyte transformation and T-lymphocyte rosettes. Women with early gestation and patients with GTN stage O revealed a significant decrease in DNCM skin reaction, 3H-thymidine uptake of PHA-stimulated lymphocytes and the proportion of peripheral lymphocytes as compared with the healthy non-pregnant controls. Patients with GTN stage I-IV revealed a significa nt reduction of total lymphocyte count, DNCB reactivity, rosette formation and 3H-thymidine uptake of PHA-stimulated lymphocytes, especially in advanced stages. Patients with initially low cell-mediated immunity exhibited poor responses to the anti-cancer chemotherapy. Autologous serum added to lymphocyte transformation in early pregnancy and trophoblastic neoplasia, but not in healthy non-pregnant controls. It is postulated this decreased cell-mediated immunity of pregnant women and GTN is due to human chorionic gonadotropin. (no Refs)

## 32. DEPRESSED CELLULAR IMMUNITY IN HEPATOCELLULAR CARCINOMA PATIENTS.

**Lee CS, Chang KJ, Lin TY, Hsieh KH, Tung TC**
**Dept. Surgery, Coll. Medicine, Natl. Taiwan Univ., Taipei, Taiwan**
**Taiwan I Hsueh Hui Tsa Chih; 80(8):780-785 1981**

The techniques of sheep RBC rosette formation (E rosettes) and sheep RBC-antibody-complement formation (EAC rosettes) were used to study lymphocyte subpopulations in 40 patients with hepatocellular carcinoma (HCC) and in 120 age- and sex-matched normal controls. In the peripheral blood, E rosette-forming T cells comprised 49.18 +-10.92% of the lymphocytes from HCC patients compared to 72.00 +-11.50% in controls (p less than 0.001). EAC rosette B cells comprised 24.0% of the lymphocytes in both groups. The mitogenic index in the phytohemagglutinin-stimulated lymphocytes of 20 HCC patients was 12.26 +-17.82 (range 0.80-35.40) compared to 83.00 +-21.70 (range 18.00-124.80) in 40 controls. Serum alpha-fetoprotein (AFP) was determined in the 40 HCC patients. In the 28 with positive response, T cell count was 50.68 +-10.40% compared to 45.67 +-12.31% in 12 with negative response. The difference was not significant. Among 20 HCC patients tested for lymphocyte transformation, serum AFP was positive in 13 and negative in 7; mitogenic indices were 16.39 +-20.77 and 4.59 +-6.11, respectively. The difference was not significant. The significance of the low T cell count in peripheral blood of HCC patients is discussed. (16 Refs)

## 33. ANTI-IMMUNOGLOBULIN-INDUCED POTASSIUM FLUX IN RELATION TO CAPPING AND DNA SYNTHESIS: AN ANALYSIS IN MONOCLONAL HUMAN B LYMPHOMA CELL POPULATIONS.

**Heikkila R, Godal T, Henriksen A, Iversen JG**
**Inst. Physiology, Oslo Univ., Oslo 1, Norway**
**Exp Cell Res; 136(2):447-454 1981**

F(ab')2 anti-u as well as anti-delta and anti-gamma heavy chains have been found to induce strong increases in the influx of 86Rb+ (a potassium analogue) in cell suspensions from a proportion of human lymphomas staining monoclonally for B cells. The specificity of the response corresponded to the surface immunoglobulin (sIg) isotype present on lymphoma cells. Even when carried out under closely analogous conditions, no relationship between capping and 86Rb+ influx was observed. On the other hand, an association between 86Rb+ influx and mitogenic response to anti-immunoglobulin (anti-Ig) was observed with concordant results in 19 out of 21 comparisons made. These findings suggest that 86Rb+ influx, which appears to be associated with mitogenic signals, and capping may arise as independent phenomena even when elicited through the same membrane receptor (sIg). (Author abstract) (27 Refs)

## 34. THE CAPPING OF LIPOSOMES ON THE SURFACE OF MURINE LYMPHOID AND LEUKEMIC CELLS.

**Rader RL, Bourguignon LY**
**Dept. Immunology and Microbiology, Wayne State Univ. Sch. Medicine, Detroit, MI, 48201**
**Cell Mol Biol; 27(2/3):215-221 1981**

Distearoylphosphatidylcholine (DSL) liposomes containing 6-carboxyfluorescein were incubated with murine splenic and leukemic lymphocytes at 4 C. Upon immediate observation at room temperature, fluorescent liposomal caps were found on a majority of the spleen cells. In marked contrast to the spleen lymphocytes, the DSL liposomes appeared to bind to the entire surface of the EL4 leukemic cells giving rise to fluores-

cent rings. After incubation of the latter cells at 37 C, the fluorescent DSL liposomes formed patches and ultimately fluorescent liposomal caps. Thus, the kinetics of liposomal capping was considerably slower in the case of the leukemic cells. Much or all of the fluorescent liposomes could be removed from both the spleen and EL4 leukemic lymphocytes by exposure of the cells to low levels of trypsin. Furthermore, the effect of various inhibitors indicated that the liposomal capping process appeared to require the involvement of both microfilaments and a source of energy. These observations suggest that the DSL liposomes had bound to the cell surfaces primarily by trypsin-sensitive sites. In addition, the results indicate that the formation of liposomal caps depends on the redistribution of the liposomes over the surface of the cells by mechanisms similar to those involved in antibody or lectin-induced capping processes. (Author abstract) (22 Refs)

### 35. IMMUNO-ELECTRON MICROSCOPY OF 'T' CELLS IN LARGE PLAQUE PARAPSORIASIS.

McMillan EM, Wasik R, Martin D, Donaldson M, Everett MA
Dept. Dermatology, Univ. Oklahoma, Health Sciences Center, 619 N.E. 13th, Oklahoma City, OK, 73104
J Cutan Pathol; 8(5):385-392 1981

The peroxidase-antiperoxidase technique was used to demonstrate a specific surface human T lymphocyte antigen (HTLA) in atrophic large plaque parapsoriasis. Tissue specimens obtained from a 55-yr-old man with a 6-yr history of parapsoriasis were prefixed in paraformaldehyde before freezing, treated with anti-HTLA, and examined by transmission electron microscopy. Positive membranous staining indicating the presence of HTLA was observed in 70% of cells. A high proportion of cells had convoluted nuclei; approx 80% of cells with convoluted nuclei were HTLA positive. The findings suggest a relationship betwee n the atrophic large plaque parapsoriasis and mycosis fungoides. (27 Refs)

### 36. APPLICATION OF CYTOTOXIC TEST FOR LYMPHOCYTE IDENTIFICATION IN ELECTRON MICROSCOPY.

Brelinska R, Jaroszewski J, Kukulska J, Rossowski W, Warchol JB
Dept. Histology and Embryology, Medical Sch. and Inst. Human Genetics, Polish Acad. Sciences, Poznan, Poland
Folia Histochem Cytochem (Krakow); 19(3):44-45 1981

Trypan blue complexed with Co, Po, Cu, or Ca ions was tested for identification of surface-antigen-carrying cells in electron microscopy. Peroxide, chlorate, and phosphate ions in free form were also tested for the same purpose. Each method is discussed and the results compared. False positive reactions can be excluded from the analysis via appropriate controls and analysis of cell ultrastructure to identify advanced alterations due to cell damage. (no Refs)

## LYMPHOCYTE AND DIFFERENTIATION ANTIGENS

### 37. HUMAN T CELL LEUKEMIA ANTIGENS ON THE CELL MEMBRANES: PURIFICATION, MOLECULAR CHARACTERIZATION, AND PREPARATION OF SPECIFIC ANTISERA.

Seon BK, Negoro S, Minowada J, Yoshizaki K
Dept. Immunology Res., Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
J Immunol; 127(6):2580-2588 1981

Human T cell leukemia-associated (HTL) antigens were isolated from cell membranes of two T leukemia cell lines, MOLT-4 and JM, without using radiolabeling. We isolated milligram quantities of a human leukemia-associated cell membrane antigen preparation that contained a single immunodominant glycoprotein of 100,000 mol wt composed a single polypeptide chain. This 100,000 mol wt glycoprotein together with the 54,000 mol wt glycoprotein are the first reported human leukemia-associated cell membrane antigens that were identified as isolated proteins without the aid of radiolabel markers. (54 Refs)

### 38. ANTIGENS DISPLAYED ON MURINE B LYMPHOCYTE PRECURSORS.

Kincade PW, Lee G, Watanabe T, Sun L, Scheid MP
Sloan-Kettering Inst. Caner Res., 145 Boston Post Road, Rye, NY, 10580
J Immunol; 127(6):2262-2268 1981

The surface antigen phenotype of the immediate precursors of clonable B Lymphocytes was investigated with conventional alloantisera and monoclonal antibodies directed to B lineage antigens. Ia was demonstrable on B cells, but not their immediate precursors in adult marrow. Adult, but not fetal, B cell precursors were susceptible to lysis with anti-Lyb-2 or Anti-Qa. A panel of monoclonal rat antibodies was prepared and placed into categories on the basis of recognition patterns obtained with established cell lines. Of two groups that are described here, in one (typified by antibodies from clone 14.8) we detect an antigen that is preferentially expressed on B cells and their precursors, a proportion of antibody-secreting cells, and a subpopulation of peripheral T lymphocytes. Cells that did not display demonstrab le amounts of antigen include brain, granulocytes, macrophages, mastocytoma cells, and erythroleukemia cells. A second category of antibodies revealed an antigen that was more widely distributed on hemopoietic cells. Cells capable of quickly maturing into functional, colony-forming B lymphocytes in culture or after transfer to irradiated recipients specifically adhered to 14.8 antibody-coated, polystyrene petri dishes in the cold. Reductions in numbers of stem cells (CFU-s) and myeloid progenitors (CFU-c) by this treatment were minimal. Of particular importance was the fact that these antibodies recognized cells in embryonic liver as well as in adults that were destined to become B lymphocytes. These observations provide new perspective on B lineage precursor heterogeneity and suggest ways of localizing and dissecting some of the earliest events that are critical to development of the humoral immune system. (Author abstract) (51 Refs)

## 39. MYELOID DIFFERENTIATION ANTIGEN DEFINED BY A MONOCLONAL ANTIBODY.

Majdic O, Liszka K, Lutz D, Knapp W
(c/o Knapp), Inst. Immunology, Borschkegasse 8A, A-1090, Vienna, Austria
Blood; 58(6):1127-1133 1981

A monoclonal antibody of the IgM kappa type directed at a determinant on K-562 cells was produced and characterized. This hybridoma antibody, provisionally termed D5, defines a membrane-associated antigen that seems to be restricted, within the hemopoietic system, to the granulocytic cell lineage and possibly also to very immature erythroid and monocytic cells. Within the granulocytic cell lineage, D5 antibody reacts with all differentiation stages starting from the promyelocyte up to and including the mature granulocyte. Normal and malignant myeloblasts are only weakly positive or negative. Within the monocytic cell lineage, only fairly immature malignant cells as represented by cells from two patients with monoblastic leukemia and by two monoblastoid cell lines were found to be strongly D5 positive. Among the mature glass-adherent monocytic cells from normal peripheral blood, only very few cells react with D5 antibody. The fact that we have raised this antibody against cells (K-562) that are considered to represent very immature erythroid precursor cells would suggest that normal erythroid precursors should also be D5 positive. However, so far we are unable to detect such cells. Therefore, the proportion of D5-positive erythroid precursors resembling the K-562 cell type must either be very low in the bone marrow, or the D5 antigen is not present on normal erythroid precursor cells and only aberrantly expressed on K-562 cells. Mature erythrocytes are also D5 negative. There was no evidence that lymphoid precursors react with D5 antibody, in that all normal and malignant lymphoid cells tested so far were D5 negative. Further, platelets showed no reactivity wi th D5 antibody. (Author abstract) (40 Refs)

## 40. SOMATIC CELL HYBRID ANALYSES OF HEMATOPOIETIC DIFFERENTIATION.

Koeffler HP, Sparkes RS, Billing R, Klein G
Dept. Medicine, Div. Hematology-Oncology, Univ. California Los Angeles Center Health Sciences, Los Angeles, CA, 90024
Blood; 58(6):1159-1163 1982

A differentiated cell expresses an entire set of specialized features. Somatic cell hybridization provides a method to examine control of gene regulation. We studied the expression of tissue-specific features in hybrids between human promyelocytes (HL-60) and human Burkitt's lymphoma cells (P3HR-1). Two hybrid lines, HP-1 and HP-2, and 18 hybrid clones were established and confirmed by karyotype, isozyme, and surface antigen analyses. The hybrids extinguished the 10 myeloid (HL-60) features that we examined including myeloid morphology, histochemistry, and functions that included response to colony-stimulating factor and ability to differentiate to granulocytes or macrophages. In contrast, the hybrids synthesized immunoglobulin and expressed Epstein-Barr nuclear, early, and viral capsid antigens similar to the P3HR-1 lymphoid parental line. Results are contrasted to the findings when P3HR-1 lymphocytes are fused to human erythroid-myeloid cells (K562). Taken together, our results suggest that phenotypic differences between human myeloid and lymphoid cells in the hematopoietic lineage involve mutually exclusive programs and may possibly be mediated by the activity of diffusible, transacting molecules. (Author abstract) (28 Refs)

## 41. HEMATOPOIETIC CELLS TRANSFORMED IN VITRO BY REVT AVIAN RETICULOENDOTHELIOSIS VIRUS EXPRESS CHARACTERISTICS OF VERY IMMATURE LYMPHOID CELLS.

Beug H, Muller H, Grieser S, Doederlein G, Graf T
Institut fur Virusforschung, Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, 6900 Heidelberg, W. Germany
Virology; 115(2):295-309 1981

REVT (avian reticuloendotheliosis virus) is a replication defective acute leukemia virus possessing a transformation-specific sequence designated rel. Hematopoietic cells transformed by REVT in vitro expressed cell surface markers of immature B lymphocytes. Some clones of transformed cells also expressed cell surface determinants of immature T lymphocytes. An antiserum specific for REVT-transformed cells reacted with the cell surface of lymphoid leukemia cells of both the B- and T-cell lineage as well as with a subpopulation of cells in normal spleen, thymus, and bone marrow. REVT-transformed cells did not express surface or cytoplasmic immunoglobulin chains nor terminal deoxynucleotidyl transferase, nor were they susceptible to infectious bursal disease virus. As expected, they were also negative for the expression of all erythroid and myeloid differentiation parameters tested. (Author abstract) (53 Refs)

## 42. SUPPRESSOR CELL ACTIVITY OF FERRITIN-BEARING LYMPHOCYTES IN PATIENTS WITH BREAST CANCER.

Moroz C, Kupfer B
Rogoff-Wellcome Medical Res. Inst., Beilinson Medical Center, 49100 Petah Tikva, Israel
Isr J Med Sci; 17(9/10):879-881 1981

In patients with early stages (I, II) of breast cancer we identified a subset of circulating lymphocytes that carry ferritin on their surface. No such lymphocytes were identified in normal women nor in women with benign breast disease. These cells did not form spontaneous rosettes with sheep red blood cells. Further studies revealed that in vitro treatment of the patients' lymphocytes with levamisole resulted in the removal of the surface ferritin and in an increase in the reactivity of the lymphocytes in mixed lymphocyte culture (MLC). Separation of the ferritin-positive lymphocytes from the E-rosetting T cells resulted in an increased reactivity of the patients' T cells in MLC. Readdition of the fraction containing the ferritin-positive cells to a mixed lymphocyte culture resulted in a decrease in the proliferative response of the patients' T lymphocytes. It is suggested that the ferritin-positive lymphocytes in breast cancer patients represent an active suppressor cell subset. (Author abstract) (13 Refs)

## 43. PHENOTYPES OF HUMAN NATURAL KILLER CELL POPULATIONS DETECTED WITH MONOCLONAL ANTIBODIES.

Zarling JM, Clouse KA, Biddison WE, Kung PC
Univ.. Minnesota Medical Sch., Box 724 Mayo Memorial Building, Minneapolis, MN, 55455
J Immunol; 127(6):2575-2580 1981

In our recent studies, human natural killer (NK) cell activity was found to be decreased two- to four-fold after treatment of monocyte-depleted peripheral mononuclear cells with monoclonal antibody OKM1 and complement (C). The present study was undertaken to determine whether there is an additional population of NK cells that is OKM1-, since treatment

with OKM1 and C decreased, but did not eradicate, NK cell activity. Treatment of lymphocytes with monoclonal antibody OKT11A, which reacts with all sheep red blood cell rosetting lymphocytes, and C also decreased NK cell activity. Although approximately 90% of OKT11A+ cells are OKT3+, NK cell activity resides within the OKT11A+ cell population, which is OKT3-since OKT3-cell depletion fails to decrease NK cell activity. Double fluorescence analysis of OKT3-depleted lymphocytes revealed that 54% of the OKM1+ cells are OKT11A- and 45% of the OKT11A+ cells are OKM1-, thus demonstrating that within the OKT3-depleted population, approximately one-half the OKM1+ cells are OKT11A- and vice versa. Treatment of lymphocytes with OKM1 together with OKT11A and C decreased NK cell activity against three NK-sensitive leukemia lines-K562, MOLT-4, and HSB-2 more than did treatment with either antibody alone; virtually no lytic activity was retained after elimination of OKM1+ and OKT11A+ cells. The results thus provide strong evidence that there are at least two populations of human NK cells; one is OKM1+ and the other is OKT11A+. (Author abstract) (19 Refs)

### 44. ANTIGEN-SPECIFIC AND NONSPECIFIC SUPPRESSOR FACTORS DERIVED FROM T CELL HYBRIDOMAS: THEIR FUNCTION AND MOLECULAR ORGANIZATION.

**Taniguchi M, Takei I, Saito T, Igarashi M, Kurihara K, Tomioka H**
**Dept. Immunology, Sch. Medicine, Chiba Univ., Chiba, Japan**
**Int Arch Allergy Appl Immunol; 66(Suppl1):204-211 1981**

A study presenting the functional and molecular organization of antigen-specific suppressor factor and some characteristics of I-J bearing antigen-nonspecific suppressor factor is discussed. With the use of the cell hybridization technique, three groups of I-Jb+ T cell hybrid lines with different functional specificities have been established. Some hybrids (34S-18, 34S-704) display an antigen-specific activity, suppressing the IgG response to DNP-KLH (dinitrophenyl-keyhole limpet hemocyanin). Some (34S-44, 34S-15) have an antigen-nonspecific activity, suppressing the IgG response to DNP-egg albumin as well as DNP-KLH. Other cell lines (34S-281, 1L-5), which have I-Jb determinants on their cell surface, showed no suppressive activity. Since suppressive activity was found in the extracted materials of the hybridomas or in the ascitic fluid from the hybridoma-bearing mice, such extracts or ascites were used for further characterization of the antigen-specific or nonspecific suppressor T cell factors (TsF). The studies reported indicate that there are closely linked I-J subregion loci coding for the determinants on the cell surface of different subsets of T cells. Further analysis indicates the possible interrelationships between I-J positive hybridomas. In the authors' laboratory, the acceptor T cell hybridoma after being stimulated by the specific TsF secretes another factor, activating the efferent limbs of the suppressor cell interaction, in which antigen-specific or nonspecific pathways are involved. (23 Refs)

### 45. CELL SURFACE ANTIGENS OF X-RAY INDUCED LYMPHOMA: DETECTION AND CHARACTERIZATION USING MONOCLONAL ANTIBODIES (MEETING ABSTRACT).

**Allison JP**
**The University of Texas System Cancer Center, Science Park, Smithville, TX, 78957**
**Hybridomas and Cellular Immortality (Second Houston Symposium), November 5-6, 1981, Houston, Texas. University of Texas Medical School at Houston 55 pp., 1981.**

The cell surface antigenic mosaic of an x-ray induced lymphoma of C57BL/6 mice has been examined using conventional and monoclonal antibodies. The tumor cells display four glycoproteins related to murine leukemia virus (MuLV) - two env and two gag gene products. Immunization of syngeneic mice with tumor cells elicited formation of antibodies to only one of the two MuLV env proteins. Analysis with monoclonal antibodies revealed that this antigen was antigenically related to ecotropic MuLV. One hybridoma clone, designated 124-40, produced by fusion of spleen cells from C6XL-immunized BALB/c mice with P3 myeloma cells, secreted monoclonal antibodies (McAb) which reacted with tumor cells, but not with normal lymphoid cells. The tumor associated antigen reative with McAb 124-40 was found to be a glycoprotein with subunit mol wt of approx 40 Kd, and was structurally and immunologically distinct from MuLV antigens on the tumor cells. The antigen was not found on adult spleen, thymus, bone marrow, or lymph node cells, nor on fetal thymus or spleen. Two additional x-ray lymphoma lines, as well as three spontaneous leukemias of AKR mice, were also unreactive with McAb 124-40. Administration of the McAB 124-40 to tumor-bearing mice resulted in a slight increase in survival time. The therapeutic effect was greatly enhanced by administration of McAb conjugated to the cellular toxin pokeweed antiviral protein. (no Refs)

## CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION

### 46. NEW CONCEPTS OF HUMAN LYMPHOID DIFFERENTIATION: IMPLICATIONS FOR UNDERSTANDING HEMATOLOGIC MALIGNANCIES (MEETING ABSTRACT).

**Reinherz EL**
**Harvard Medical School, Boston, MA, 02115**
**VIII Conference on Analytical Cytology and Cytometry, May 19-25, 1981, Wentworth-by-the-Sea, New Hampshire Memorial Sloan-Kettering Cancer Center; 1981**

The ability to define cell surface antigens that appear at specific stages of lymphoid differentiation has allowed for the orderly dissection of many human hematologic malignancies. In fact, these diseases reflect the same degree of heterogeneity and maturation as seen in normal ontogeny. For example, the tumor cells in most cases of acute T cell lymphoblastic leukemia arise from an early thymocyte or prothymocyte compartment (Stage I) whereas approx 20% of the cases have cells derived from a common thymocyte compartment (Stage II) and therefore bear the TL-like antigen, T6. To date, we have found only a few T cell acute lymphoblastic leukemia tumors that arose from the most mature thymic compartment and expressed the T3 antigen (Stage III). Since normal thymocytes

have not required mature T cell functions at either the level of Stage I or Stage II thymocytes, it is not suprising that the vast majority of acute lymphoblastic leukemia T cells have no demonstrable function. In contrast, the tumor population from patients with T cell chronic lymphatic leukemia, Sezary syndrome, and mycosis fungoides are derived from the mature T cell compartment, bearing the T1 or T3 antigens or both. Therefore, as expected, some of these tumor cells display regulatory functions. In this regard, all tumor populations from patients with Sezary syndrome bear the T1+ T3+ T4+ phenotype and many demonstrate the functional capacity to provide help to B cell Immunoglobulin syn thesis. T cell Chronic lymphocytic leukemia tumor populations have mature inducer or suppressor phenotypes. Among the non-T cell leukemias, a significant percentage derive from the pre-B cell compartment. As with the T cell malignancies, monoclonal antibodies defining normal B cell surface antigens are useful in detecting heterogeneity. (no Refs)

## 47. PROTEIN GLYCOSYLATION IS REQUIRED FOR THE PROLIFERATION OF MITOGEN-ACTIVATED LYMPHOCYTES.

**Harrison ML, Villemez CL**
**Tumor Immunology, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104**
**J Immunol; 127(6):2616-2617 1981**

The biochemical events underlying the lymphocyte activation process are at present not understood, although it is clear that surface components play a crucial role. In vitro, activation can be induced by specific mitogens such as bacterial lipopolysaccharide (LPS; specific for B lymphocytes) or the plant lectin concanavalin A (Con A, specific for T lymphocytes). One result of lymphocyte mitogenesis is a dramatic increase in cellular proliferation. It is clear that the activation signal provided by the mitogen results from an initial contact between the mitogen and the lymphocyte surface, presumably through a specific membrane receptor. Other membrane components that may play an essential role in inducing or maintaining the proliferative state have not been identified. Through work involving the glycosylation of lymphocyte proteins, we observed that inhibition of protein glycosylations occurring via the lipid intermediate (dolichol) pathway resulted in the prevention of lymphocyte activation. The antibiotic tunicamycin (TM)(3) specifically inhibits glycosylations occurring via the lipid intermediate pathway. We report here that nanomolar quantities of TM prevented lymphocyte proliferation induced by either Con A or LPS. In direct contrast, TM had no effect on the proliferation of nonactivated lymphocytes, BW147.3 lymphatic leukemic cells, H4-II-E-C3 hepatoma cells, or Escherichia coli B bacteria. (Author abstract) (24 Refs)

## 48. CHANGES OF CELLULAR MARKERS DURING DIFFERENTIATION OF HL-60 PROMYELOCYTES TO MACROPHAGES AS INDUCED BY T LYMPHOCYTE CONDITIONED MEDIUM.

**Chiao JW, Freitag WF, Steinmetz JC, Andreeff M**
**Sloan-Kettering Inst. Cancer Res., 410 East 68th St., New York, NY, 10021**
**Leuk Res; 5(6):477-489 1981**

Conditioned medium (CM) derived from allogeneic or phytohemagglutinin-stimulated lymphocytes was studied for its effect on cultures of the human promyelocytic cell line HL-60 from a patient with acute promyelocytic leukemia. Adherent cells in the proportion of 3-8% were noted beginning at 10-18 hr of incubation of the cultures with the CM; the proportion increased to 5-15% by 60 hr but decreased after 3 days. The CM-treated HL-60 cells differed from untreated cells in that they gradually underwent morph ological changes indicative of differentiation. The earliest significant morphologic changes were seen after 3 days in culture; approx 25% of the cells were macrophage-like and 3% were monocyte-like. For culture days 1-3, the viability of the CM-treated cells (89%) was essentially the same as that of the cells (91%) before culturing with the CM. Continued culture with CM resulted in a further proportional decrease in promyelocytes, paralleled by a concomitant increase in monocyte- and macropnage-like cells. The findings suggested that CM-induced morphological maturation is caused by activated lymphocyte product. A decrease in HL-60 RNA content following CM culture seemed to be an early event in differentiation preceding morphological maturation. The proportion of proliferating cells decreased from 46% of the untreated cells to 13% after 7 days of CM incubation. During the culture period the CM induced the development of membrane markers and functions that were absent in the untreated population. T lymphocytes were those most responsible for production of the maturation inducer in the CM; the inducer most likely stemmed from activated T lymphocytes. (37 Refs)

## 49. EXPRESSION OF NORMAL MONOCYTE-MACROPHAGE DIFFERENTIATION ANTIGENS ON HL60 PROMYELOCYTES UNDERGOING DIFFERENTIATION INDUCED BY LEUKOCYTE-CONDITIONED MEDIUM OR PHORBOL DIESTER.

**Todd RF, Griffin JD, Ritz J, Nadler LM, Abrams T, Schlossman SF**
**Div. Tumor Immunology, Sidney Farber Cancer Inst., Harvard Medical Sch., Boston, MA, 02115**
**Leuk Res; 5(6):491-495 1981**

The acquisition of normal, nonpolymorphic surface membrane antigens Mo1 and Mo2 was demonstrated in a significant proportion of HL60 human promyelocytic cells that were induced to differentiate by WBC-conditioned medium or by the phorbol ester 12-O-tetradecanoylphorbol-13-acetate. Mo2 antigen was specific for late monocyte-macrophage differentiation and was expressed by peripheral blood monocytes and cultured macrophages but not by earlier myeloid forms including promyelocytes. The Mo1 antigen was found on mature granulocytes and null cells as well as on monocytes and macrophages. (8 Refs)

## 50. T CELL RECOGNITION OF MOLONEY LEUKEMIA VIRUS PROTEINS: III. T CELL PROLIFERATIVE RESPONSES AGAINST GP70 ARE ASSOCIATED WITH THE PRODUCTION OF A LYMPHOKINE INDUCING 20 ALPHA-HYDROXYSTEROID DEHYDROGENASE IN SPLENIC LYMPHOCYTES.

**Ihle JN, Lee JC, Rebar L**
**Biological Carcinogenesis Program, Frederick Cancer Res. Center, Frederick, MD, 21701**
**J Immunol; 127(6):2565-2570 1981**

One of the characteristic cellular immune responses associated with the regression of Moloney leukemia/sarcoma virus-induced tumors is a T cell proliferative response against the major viral envelope glycoprotein, gp70. The results described here demonstrate that associated with this proliferative response is the production of a lymphokine, Interleukin 3 (IL-3). The production of IL-3 was immunologically specific and showed the same specificity as that observed in blastogenic responses. IL-3 production was dependent upon an antigen-specific Thy-1.2+, Lyt-1+, 2-lymphocyte subpopulation but did

not require the presence of an Ia+ or an adherent accessory cell. The results also suggested that IL-3 may constitute one of the blastogenic factors previously shown to be involved in the proliferative response to gp70. In particular purified IL-3 was found to induce proliferation of both normal and immune nylon wool purified splenic lymphocytes. The phenotype of the responding lymphocyte subpopulation was Thy-1.2-, Lyt-1-, 2-, Ig-, and Ia-. Maximal IL-3 production occurred approximately 48 hr after the addition of antigen and its production was significantly blocked by mitomycin C. These characteristics were unlike those for the general production of blastogenic factor activity suggesting that IL-3 is responsible for only a minor component of the proliferative response. (Author abstract) (19 Refs)

### 51. QUALITATIVE CHARACTERISTICS OF HISTAMINE RELEASE FROM HUMAN BASOPHILS BY COVALENTLY CROSS-LINKED IGE.

**Kagey-Sobotka A, Dembo M, Goldstein B, Metzger H, Lichtenstein LM**
**Good Samaritan Hosp., 5601 Loch Raven Blvd., Baltimore, MD, 21239**
**J Immunol; 127(6):2285-2291 1981**

We have studied the effects of permanent oligomers of human IgE produced using the cross-linking reagent, dimethyl suberimidate, on histamine release from human basophils. IgE dimers were found to be sufficient stimuli for both release and desensitization of these cells; monomeric IgE had no effect. Histamine release was augmented by deuterium oxide (D2O) in the medium, but D2O was not an absolute requirement to observe release. Desensitization by the dimeric IgE was specific in that the response to anti-IgE was not affected by preincubation of the leukocytes with the IgE dimer under suboptimal releasing conditions. IgE trimers and higher oligomers of IgE also caused both release and desensitization. IgE trimers were three- to four-fold more effective than IgE dimers with regard to the amount required for 50% histamine release. Dilution studies with monomeric IgE suggested that the difference was due to the presence of more 'active' dimers in the trimeric IgE fractions. We conclude that dimeric IgE, by juxtaposing two receptors on the basophil membrane, is the 'unit signal' for both release and desensitization of these cells. (Author abstract) (22 Refs)

### 52. DESTRUCTION OF TUMOR CELLS BY MACROPHAGE PRECURSORS IN MOUSE AND MAN.

**Lohmann-Matthes ML, Zahringer M**
**Max-Planck-Institut fur Immunbiologie, Stubeweg 51, D-7800 Freiburg i. Br., W. Germany**
**Blut; 42(5):283-295 1981**

Macrophage precursors exhibiting killer cell (K-cell) and natural killer cell (N K-cell) activity were detected in vivo in mice and humans. Peritoneal exudate was induced in C57/BL10 mice by ip injection of 100 ug Corynebacterium parvum. The exudate showed K-cell and NK-cell activity against Yac-1 and DBA/2 P815X tumor cells. Separation by column adherence produced a population of nonadherent cells, consisting of small lymphocytes and middle-sized, promonocyte-like cells (PML), which had K-cell and NK-cell activity. The PML lacked nonspecific esterase (a marker for mature macrophages), but when cultured produced mature macrophages after 3 days, indicating that the cultured cells were macrophage precursors. Similar cells were isolated from spleens of nu/nu mice and from human peripheral blood. The activity of these cells was absorbed by allogeneic antimacrophage serum Mph 1.2 with rabbit complement. The cells were nonadherent and nonphagocytic. Results indicate that macrophage precursor cells, as well as mature macrophages, are released from bone marrow into peripheral circulation in mice and humans, and that these precursor cells have cytotoxic effects on tumor cells. (24 Refs) (In GER)

### 53. PHOSPHOLIPASE ACTIVATION IN THE IGE-MEDIATED AND CA++ IONOPHORE A23187-INDUCED RELEASE OF HISTAMINE FROM RAT BASOPHILIC LEUKEMIA CELLS.

**McGivney A, Morita Y, Crews FT, Hirata F, Axelrod J, Siraganian RP**
**Clinical Immunology Section, Lab. Microbiology and Immunology, Natl. Inst. Dental Res., Bethesda, MD, 20205**
**Arch Biochem Biophys; 212(2):572-580 1981**

The role of receptor-mediated phospholipase (PL) activation in histamine liberation from rat basophilic leukemia cells was examined. PL activation was necessary for IgE-mediated and ionophore-induced histamine liberation from the cells. Inhibition of PL blocked the release of histamine. Neither the lipoxygenase nor the cyclooxygenase pathway appeared essential for the initiation of histamine release. (26 Refs)

## EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS

### 54. TOXICITY, IMMUNOSUPPRESSIVE, AND CYTOTOXIC EFFECTS OF SOME ANTINEOPLASTIC AGENTS.

**Kireeva IV, Pykhtina AA, Gladkova NE, Khomchenovskii EI**
**Dept. Pharmacology, N. I. Pirogov Second Medical Inst., Moscow, USSR**
**Farmakol Toksikol; 44(6):718-721 1981**

Immunosuppressive and cytotoxic effects of the antineoplastic agents pafencil (PF), C-119, C-72, bleomycin (BL), and L-aspariginase (LAS) were studied in CBA mice. The PF, C-72, and BL were more toxic than the C-119 and LAS. The alkylating agents (PF, C-119, and C-72) provided more pronounced inhibition of antibody-producing cells and rosette-forming cells than did the BL and the LAS. The most pronounced inhibition of number of nucleated splenocytes was observed after the administration of the LAS. (17 Refs) (In RUS)

### 55. IN VITRO AND IN VIVO MODULATION OF THE IMMUNE RESPONSE OF PATIENTS BEARING SOLID TUMORS BY CIS-PLATINUM (MEETING ABSTRACT).

**Cupissol D, Favier F, Serrou B**
**Department of Chemo-Immunotherapy, Hopital St. Eloi, BP 5054, 34 033, Montpellier, Cedex, France**
**UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.**

One of the major problems facing the cancerologist is to find means by which tumor vol can be reduced and the immune response modulated in favor of the patient. A few investigators have shown that maintenance or restoration of immune responses can be correlated with an improved prognosis. We have evaluated the immunorestorative properties of cis-diamino-dichloroplatinum (CDDP). In vitro, we have observed a

significant increase in the number of auto-rosette forming cells (ARFC: T cells) and in the natural killer (NK) activity. This effect is dose dependent. In vivo, in 6 patients bearing solid tumors, we have studied the levels of delayed hypersensitvity skin tests, circulating ARFC and NK activity, before and after treatment (100 mg/m2 in IV injection). CDDP did not alter delayed hypersensitivity values when evaluated by the Merieux score method. A significant increase in ARFC was noted for all the patients treated with CCDP, and NK activity increased significantly shortly after treatment by CDDP. These results suggest that some chemotherapy drugs have to be considered as a part of the biological response modifiers. (no Refs)

### 56. LYMPHOCYTE SURFACE MARKERS DURING THE TREATMENT OF NON-HODGKIN'S LYMPHOMAS.

**Trepinska E, Burchardt K**

**Dept. Hematology, Inst. Internal Diseases, Medical Academy, Poznan, Poland**

**Z Gesamte Inn Med; 36(18):681-682 1981**

Lymphocyte populations were studied in 22 patients with non-Hodgkin's lymphoma (NHL) before and during treatment with cyclophosphamide, oncovin, procarbazine and prednisone (COPP). Null cells (without cell-membrane markers) predominated in normal individuals and untreated NHL patients. COPP treatment reduced the number of null cells, with consequent reduction in total lymphocyte count. Marker-bearing T and B cells were less affected by treatment. NHL patients in remission had increased null cell counts, but near-normal counts for marker-bearing cells. (6 Refs) (In GER)

### 57. IMMUNE IMBALANCE AND IMMUNE MODULATION IN SOLID TUMOR PATIENTS: NEW INSIGHTS.

**Serrou B, Cupissol D, Rosenfeld C**

**Laboratoire d'Immunopharmacologie des Tumeurs, Hopital Saint-Eloi, Centre Paul Lamarque, F-34033 Montpellier Cedex, France**

**Recent Results Cancer Res; 80:9-16 1982**

Immune status in patients with solid tumors is reviewed. Several studies have found a variety of immunocomplexes (IC) that are present in increasing amounts during tumor growth or relapse (TGR) and in decreasing amounts following tumor reduction (TR). Because these complexes are a pparently varied and poorly defined, practical use of IC measurements is limited. Changes in the plasma membrane lipid bilayer of WBC occur during TGR and disappear during TR. Plasma microviscosity may change in a similar fashion. Studies of patients treated with BCG have indicated that those with high levels of anti-BCG antibodies generally have a good prognosis, while those with low levels have a poor prognosis. A similar correlation has been found for vitamin A. Vitamin A apparently plays a role in cell differentiation and immune response. The T-gamma lymphocyte/T-mu lymphocyte ratio in patients increases during TGR and decreases during TR. A T-theophylline-resistant lymphocyte population that forms autologous rosettes is reduced during TGR and increases during TR. Suppressor-cell activity is affected by antiprostaglandins or irradiation and has therapeutic implications. Of new immunomodulating drugs, bestatin has antitumor activity in mice and RO-109359 increases cutaneous delayed hypersensitivity; results with interferon are unclear. (28 Refs)

### 58. SPLENIC IRRADIATION IN PROLYMPHOCYTIC LEUKAEMIA (MEETING ABSTRACT).

**Oscier DG, Errington RD, Catovsky D, Goolden AW, Roberts P**

**Department of Radiotherapy, Postgraduate Medical School, Hammersmith Hospital, London, England**

**Br J Radiol; 56(644):140 1981**

Prolymphocytic leukemia (PLL) is a chronic lymphoproliferative disorder characterized by massive splenomegaly and a high peripheral blood prolymphocyte count. In the original series of 15 patients, there was a poor response to alkylating agents and steroids, and only one out of six patients benefited from splenic irradiation. We have treated a further 12 patients with B-PLL with splenic irradiation on a 60Co unit using a weekly dose of 100 centi Gray (cGY) up to max total dose of 1000 cGy. The treatment was well tolerated and had to be interrupted because of thrombocytopenia in only one patient. Seven patients responded well to treatment. In each case the white cell count fell rapidly to normal levels and spleen size diminished throughout the treatment period. Five of the responding patients remain well from 6 mo to 8 yr following splenic irradiation. One remains in complete remission 18 mo post-splenectomy, following a second course of splenic irradiation, while two have died of unrelated causes. Four of the five non-responders have died as a result of their disease. Those patients whose peripheral blood prolymphocytes form more than 25% of mouse RBC rosettes seem more likely to respond. We consider that splenic irradiation should be the primary form of treatment for the majority of patients with PLL. (1 Ref)

### 59. SEZARY SYNDROME WITH A 14:14 (Q12:Q31) TRANSLOCATION.

**Shah-Reddy I, Mayeda K, Mirchandani I, Koppitch FC**

**Wayne State Univ. Sch. Medicine, Hutzel Hosp., 4707 St. Antoine, Detroit, MI, 48 201**

**Cancer; 49(1):75-79 1982**

The Sezary syndrome was diagnosed in a 71-yr-old black woman with erythroderma, generalized lymphadenopathy and hepatosplenomegaly. The laboratory data revealed a WBC count of 65,000 mm3 with 81% lymphocytes, the majority having an indented or a cerebriform nucleus. The skin biopsy, the lymph node biopsy and immunologic surface marker studies confirmed the diagnosis of Sezary syndrome. The cytogenetic studies of the bone marrow and the peripheral blood revealed a (14:14) (q12:q31) translocation present, consistently in majority of the lymphocytes. This translocation is considered characteristic of ataxia-telangiectasia and, to our knowledge, has not been previously described in Sezary Syndrome. (Author abstract) (31 Refs)

## OTHER RELATED STUDIES

### 60. IN VITRO GROWTH OF LYMPHOMA COLONIES FROM CHILDREN WITH NON-HODGKIN'S LYMPHOMA.

**Smith SD, Wood GW, Fried P, Lowman JT**

**Dept. Pediatrics, Univ. Kansas Medical Center, Kansas City, KS, 66103**

**Cancer; 48(12):2612-2623 1981**

Growth in vitro of malignant lymphoid cells has been previously reported, but those studies involved direct establishment of cell lines from the patients' cells. In the present study, an in

vitro system for both primary growth and passage of malignant lymphoblastic colony-forming cells (ML-CFC) was established, and for the first time, colony-forming cells from non-Hodgkin's lymphoma patients were cultured, and cell lines were established from individual colonies. Malignant lymphoid colonies grew from 9 of 16 (56%) bone marrow aspirates, which were histologically involved with lymphoma and from 5 of 29 (17%) morphologically normal bone marrow samples. ML-CFCs grew concomitantly with myeloid and monocytic CFCs and were distinguishable by their morphologic characteristics on agar, cytochemical staining characteristics, and cell surface markers. Successful passage of ML-CFCs was accomplished in five patients, and 10 distinct cell lines (6 null cell, 3 B cell, and 1 T cell) were established. This agar assay system provides an opportunity to study malignant lymphoma cell growth both as a primary colony and as a cell line established from a primary colony. (Author abstract) (44 Refs)

## 61. TYPE C VIRUS PARTICLES IN A CORD T-CELL LINE DERIVED BY CO-CULTIVATING NORMAL CORD LEUKOCYTES AND HUMAN LEUKAEMIC T CELLS.

**Miyoshi I, Kubonishi I, Yoshimoto S, Akagi T, Ohtsuki Y, Shiraishi Y, Nagata K, Hinuma Y**
**Dept. Medicine, Kochi Medical Sch., Kochi 781-51, Japan**
**Nature; 294(5843):770-771 1981**

Cocultivation of adult T-cell leukemia (ATL) cells with cord WBC from a male infant was used to establish a T-cell line that expresses ATL-associated antigens (ATLAs) and contains numerous C-type virus particles. The ATLAs were detected by indirect immunofluorescence using ATL patients' sera and fluorescein isothiocyanate-conjugated goat antihuman IgG. Thin-section electron microscopy revealed the virus particles, which are predominantly mature and consist of an electron-dense nucleoid and an outer membrane. (8 Refs)

## 62. EXPERIMENTAL AND CLINICAL STUDIES OF IMMUNOLOGICAL ACTIVITY OF MONOCYTES IN TUMOR-BEARING HOSTS. I. KINETICS OF PERITONEAL MACROPHAGE FUNCTIONS IN TUMOR-BEARING MICE.

**Yamada Y**
**Dept. Surgery, Res. Inst. Nuclear Medicine and Biology, Hiroshima Univ., Kasumi, Hiroshima 734, Japan**
**Hiroshima Daigaku Igaku Zasshi; 29(3):491-502 1981**

The immunological reactivity of nonactivated and Corynebacterium parvum (C parvum)-activated peritoneal macrophages in tumor-bearing mice was investigated in relation to several macrophage functions - chemotaxis, phagocytosis, cytostasis, cytolysis and serum lysozyme activity. Peritoneal exudate cells (PEC) decreased from Day 14 after tumor inoculation and more significantly at day 28. The number of PEC from tumor-bearing mice treated with C parvum increased, but, in the late stage, less than in normal C parvum-treated mice. The response to WBC-derived chemotactic factor was significantly depressed in the early stage of the tumor-bearing mice and did not recover until the late stage. It was increased by injection of C parvum, but less after Day 7 than that of C parvum-treated normal mice. Phagocytosis of latex beads increased significantly within 10 days after tumor inoculation, then progressively decreased to normal and remained normal until death. It was increased by C parvum as much as that from C parvum-treated normal mice. Cytostatic activity of tumor-bearing mice increased in the early stage, then decreased. It seemed to be related to immunocompetence and prognosis of tumor-bearing mice. C parvum increased the even activity in the late stage. Cytolytic activity of tumor-bearing mice was initially absent, but became apparent when the tumor grew, reached a max on Day 10 and decreased in the late stage. It was enhanced by C parvum, but less in tumor-bearing mice than in normal mice. Serum lysozyme activity, a possible marker of macrophage function, showed a small increase in tumor-bearing mice but no further progression. It either increased or decreased after treatment with C parvum. (Author abstract) (39 Refs) (In JPN)

## 63. INDUCTION OF LYMPHOMAS AND TUMOR ANTIGEN BY MAREK'S DISEASE VIRUS IN TURKEYS.

**Elmubarak AK, Sharma JM, Witter RL, Nazerian K, Sanger VL**
**U. S. Dept. Agriculture, SEA-AR, Regional Poultry Res. Lab., 3606 E. Mount Hope Road, East Lansing, MI, 48823**
**Avian Dis; 25(4):911-926 1981**

Mycoplasma-free turkeys were inoculated with the highly pathogenic GA isolate of Marek's disease (MD) virus (MDV), and were observed for lympholytic and lymphoproliferative lesions and humoral and cellular immunocompetence. Inoculated turkey poults became persistently viremic with MDV, with levels of circulating MDV that were lower than in similarly inoculated specific-pathogen-free chickens. The early lytic phase of MD with lymphoid cell destruction and appearance of viral antigen in lymphoid organs was less pronounced than in chickens. Gross lesions in turkey poults after MDV infection were most frequent in spleen and liver but also involved kidneys, gonad, heart, thymus, and peripheral nerves. MD tumors contained cells that reacted with antiserum prepared against chicken MD-tumor-associated surface antigen. This result indicated that MDV induced cellular transformation in turkeys and that the tumor-associated antigen in chickens and turkeys cross-reacted. Several in vitro-propagating B-cell lines were developed from turkey lymphomas. MD in turkeys resulted in immunodepression as it did in chickens. Circulating lymphocytes from turkeys that eventually died of MD or had developed gross tumors were deficient in response to Concanavalin A. (19 Refs)

## 64. DYNAMICS OF IMMUNE REACTIVITY IN PATIENTS WITH ENDOMETRIAL AND CERVICAL CARCINOMA (MEETING ABSTRACT).

**Bolanca M, Vecek N, Jurin M**
**Department of Obstetrics and Gynecology, Medical School, University of Zagreb, Zagreb, Yugoslavia**
**UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.**

The pronounced depression of the immune response present in organism with tumor led us to study the dynamics of immunological reactivity in patients with gynecological (cervical and endometrial) carcinoma prior to, during and every 3 mo after therapy. Transformation of patients' lymphocytes with phytohemagglutinin (TL-PHA) and the level of IgG in the sera were determined. Until now, 104 patients with cervical and 64 with endometrial carcinoma have been followed, most of them for 3 yr. Prior to therapy TL-PHA values were diminished significantly in about 75% of the patients, regardless of the age of the patients and the stage of disease. Simultaneously IgG values were elevated. During therapy, TL-PHA levels were more decreased even in patients with initially normal values. IgG values, however, were still elevated. The patients who died following therapy had permanently low TL-PHA values and in some the IgG levels were also decreased. Surviving patients formed two groups. In one, TL-PHA values nor-

malized faster in younger patients with less advanced disease, and in the other group, in spite of satisfactory gynecological findings, TL-PHA values remained low for 2 yr. Immunological monitoring is still in progress. IgG values were normal in both groups. In 14 of the patients with recovered TL-PHA response the response decreased either parallel with tumor regrowth or with metastases. Sometimes it preceeded tumor regrowth. These preliminary data indicate the potential usefulness of immunological monitoring in cancer patients to evaluate the effect of therapy. (no Refs)

## 65. CLINICAL STUDY OF ESTROGEN RECEPTOR IN CHINESE PATIENTS WITH BREAST CANCER.

**Liu TJ, Chi CW, Cheng EC, Chyr R, Lee C, P'Eng FK**
**Div. General Surgery, Dept. Surgery, Veterans General Hosp., Taipei, Republic of China (Taiwan)**
**Taiwan I Hsueh Hui Tsa Chih; 80(9):909-918 1981**

Preliminary studies of the correlation between tumor estrogen receptor (ER) contents and clinical response to endocrine manipulation of 126 recurrent or metastatic breast cancer patients and use of primary cancer specimens to predict hormone dependency of potential metastases are described. Positive ER levels were found in 16/43 Stage I specimens, 11/37 Stage II, 12/16 Stage II, and 7/10 Stage IV. Of the 106 primary and 20 secondary cancer patients, 46 and 5, respectively, were ER+. In the secondary cancer group, 4/16 locally recurrent or chest wall specimens, 1/2 lung and pleural cavity specimens, and 0/2 of cervical lymph nodes from patients with advanced metastatic breast cancer were ER positive. The mean of positive ER was higher in the postmenopausal group (62.85 +-13.91 vs 38.28 +-8.12 femtomole/mg cytosol protein). The same pattern was found in negative ER cases (2.77 +-0.50 vs 1.86 +-0.52 femtomole/mg cytosol protein). Both male breast cancer specimens were ER+. Of 30 benign breast cancer specimens examined, 6 were ER+. Hormonal treatment of 26 patients produced a fairly high response rate in ER+ patients. Ablative therapy was performed in 12 patients (6 ER+ and 6 ER-). All 5/5 ER+ and 0/5 ER- patients responded to oophorectomy. Neither ER+ nor ER- patients responded to bilateral adrenalectomy. Tamoxifen treatment produced responses in 3/5 ER+ and 0/2 ER- patients. Combined therapy with oophorectomy and tamoxifen also produced a good response in two ER+ patients. One ER+ and 1/2 ER- patients responded to oophorectomy and testosterone treatment. Therapy complications are described. Results indicated that the cytoplasmic ER assay in breast cancer patients is a reliable indicator for selection of good responders to hormonal treatment. (25 Refs)

## 66. ROLE OF ANTIBODY IN CYTOTOXICITY BY LYMPHOCYTES ARMED AGAINST 253J BLADDER CANCER LINE.

**Catalona WJ, Ratliff TL, McCool RE, Heston WD**
**Surgery Res., Jewish Hosp. St. Louis, 216 South Kingshighway, St. Louis, MO, 63110**
**Int Arch Allergy Appl Immunol; 66(3):259-266 1981**

The role of antibody-dependent cell-mediated cytotoxicity (ADCC) in cytotoxicity mediated by antibody-armed effector cells was examined. Cytotoxicity mediated by unsensitized human peripheral blood mononuclear cells (MNC) directed against the human bladder cancer cell line, 253J, was significantly enhanced when MNC were preincubated with a rabbit anti-253J serum and then washed free of unbound antib ody. Non-adherent, Fc receptor positive MNC were the effector cells and the arming antibody was IgG. Supernatants of 24-hr cultures and armed MNC exhibited antibody activity in ADCC assays, suggesting the ADCC was in part responsible for the arming phenomenon. (Author abstract) (23 Refs)

## 67. ANTIGEN-DRIVEN HELPER CELL-INDEPENDENT CLONED CYTOLYTIC T LYMPHOCYTES.

**Widmer MB, Bach FH**
**Immunobiology Res. Center, Univ. Minnesota, Box 724 Mayo Memorial Building, Minneapolis, MN, 55455**
**Nature; 294(5843):750-752 1981**

Cellular interactions between alloreactive cytolytic T lymphocytes (CTLs) and helper T cells have been suggested by the results of experiments in which lymphocyte subpopulations were defined by antisera against cell-surface markers or by differential response to antigenic stimulation. The development of T-cell cloning technology has allowed the isolation of alloreactive cloned helper and cytolytic cells, and the demonstration of collaboration between them in the generation of cytotoxicity. Whereas some types of alloantigen-specific cloned T cells, including helper cells, proliferate in tissue culture in response to antigenic stimulation, CTLs isolated thus far do not and require for proliferation the addition of exogenous T-cell growth factors (TCGFs) or helper cells which produce TCGF in response to antigenic stimulation. We demonstrate here, at the clonal level, the existence of another type of CTL which proliferates in response to allogeneic stimulating cells without the overt addition of TCGF; it produces helper-like factor and thus can be characterized as a helper cell-independent CTL. (Author abstract) (14 Refs)

## 68. OSTEOSARCOMA PATIENTS: ISOLATION OF SERUM ANTIBODIES BY AFFINITY CHROMATOGRAPHY.

**Tsang KY, Fudenberg HH, Gnagy MJ**
**Dept. Basic and Clinical Immunology and Microbiology, Medical Univ. South Carolina, Charleston, SC, 29403**
**JNCI; 67(6):1183-1189 1981**

Antibodies specific for membrane-associated antigens of human osteosarcoma cells were isolated from sera of 12 patients with (OS). Affinity columns were prepared by coupling partially purified membrane antigens from cultured human OS cell lines (TE-85 or LM) to CBrN-activated Sepharose 4B. The antigens were prepared by discontinuous sucrose gradient ultracentrifugation, papain digestion, and DEAE column chromatography. Diluted serum was passed over the affinity columns, and the adsorbed proteins were eluted with 2.5 M MgCl2 (pH 6.5). Immunodiffusion, indirect immunofluorescence, and complement fixation were used to assay antibody activity in the eluate. Specific anti-OS activity was found in the immunoglobulin (Ig) fraction isolated from the sera of the 12 OS patients, as confirmed by blocking experiments. No anti-OS antibody activity was found in sera from healthy individuals or patients with breast carcinoma, clear cell carcinoma, lip osarcoma, or leukemia in this study. The anti-OS activity of the isolated Ig from OS patients was abolished after absorption with cultured human OS cells from lines LM, TE-85, or G292 but not after absorption with cells from lines WI-38 (embryonic lung), TE-32 (rhabdomyosarcoma), CAMA-1 or SW527 (breast carcinoma), or M-14 (melanoma). Absorption with rabbit antihuman IgG but not with rabbit antihuman IgM immunobeads completely eliminated the antibody activity. (Author abstract) (36 Refs)

**69. T-CELL LEUKEMIA INDUCED BY 1-PROPYL-1-NITROSOUREA IN FISCHER RATS.**

**Imamura N, Saito O, Dohy H, Ogiu T**
**Dept. Internal Medicine, Res. Inst. Nuclear Medicine and Biology, Hiroshima Univ., Kasumi 1-2-3, Hiroshima, Japan**
**Experientia; 37(12):1339-1340 1981**

T-cell leukemia was induced at a high rate in female Fischer rats by continuous oral administration of 1-propyl-1-nitrosourea. No association of oncorna viruses were found in the leukemogenesis. (Author abstract) (10 Refs)

* U. S. GOVERNMENT PRINTING OFFICE : 1982—361-647/117

# AUTHOR INDEX WITH CITATION NUMBERS


Abrams T 49
Aguet M 21
Akagi T 61
Akwari AM 4
Allison JP 45
Amagasaki T 15
Anderson TC 14
Andreeff M 48
Axelrod J 53
Baccarani M 5
Bach FH 67
Bagnara G 5
Bain GO 16
Baines MG 19
Balcerzak SP 22
Baldwin RW 26
Barcos M 9
Belch A 16
Beug H 41
Biddison WE 43
Billing R 40
Blanchard B 21
Bobrove AM 17
Bolanca M 64
Bourguignon LY 34
Bradley J 7
Brelinska R 36
Brooks CG 26
Brooks D 7
Brunelli M 5
Burchardt K 56
Burke JS 10
Catalona WJ 66
Catovsky D 58
Catovsky D 7
Chamberlain JW 1
Chan JK 4
Chang KJ 32
Cheng EC 65
Cherchi M 7
Chi CW 65
Chiao JW 48
Cho BC 31
Chyr R 65
Clouse KA 43
Colby TV 10
Crews FT 53
Cupissol D 55
Cupissol D 57
Dadey B 9
Dembo M 51
Dierich MP 20
Doederlein G 41
Dohy H 69
Donaldson M 35
Dorfman RF 10
Eberle R 25
Elmubarak AK 63
Errington RD 58
Everett MA 35
Falini B 18
Favier F 55
Folds JD 4
Freitag WF 48
Fried P 60
Fudenberg HH 68
Gallinger LA 19
Gewurz H 23
Gladkova NE 54
Gnagy MJ 68
Gobbi M 5
Godal T 33
Goldstein B 51
Gomard E 27
Goolden AW 58
Graf T 41
Graninger W 6
Gray JD 26
Grieser S 41
Griffin JD 49
Griffith K 14
Gutensohn W 12
Halverson CA 18
Hammann KP 20
Han T 9
Hansen B 23
Harrison ML 47
Heikkila R 33
Henderson ES 9
Henriksen A 33
Hermina NS 22
Heston WD 66
Hild DH 17
Hinuma Y 61
Hirata F 53
Hofer F 6
Holden CA 13
Hsieh KH 32
Igarashi M 44
Ihle JN 50
Ikeda S 15
Imamura N 69
Isobe K 8
Iversen JG 33
Iwamura H 8
James K 23
Jaroszewski J 36
Jones SE 14
Jurin M 64
Kagey-Sobotka A 51
Kamihira S 15
Kanoh T 11
Kato Y 8
Kawashima K 8
Kenwrick S 26
Khomchenovskii 54
Kim SJ 31
Kincade PW 38
Kinoshita K 15
Kireeva IV 54
Kitamura T 15
Klein G 40
Knapp W 39
Koeffler HP 40
Koppitch FC 59
Koya M 11
Kubonishi I 61
Kukulska J 36
Kung PC 43
Kupfer B 42
Kurihara K 44
Lam T 1
Lee C 65
Lee CS 32
Lee G 38
Lee JC 50
Lee V 29
Levy JP 27
Lichtenstein LM 51
Lin TY 32
Liszka K 39
Liu TJ 65
Lohmann-Matthes 52
Lowman JT 60
Lutz D 39
MacDonald DM 13
Majdic O 39
Marini M 5
Martin D 35
Martin RS 17
Matutes E 7
Mayeda K 59
McCool RE 66
McGivney A 53
McKenzie IF 27
McMillan EM 35
Metzger H 51
Minami S 8
Minowada J 37
Mirchandani I 59
Miyoshi I 61
Moolten FL 24
Moon TE 14
Morita Y 53
Moroz C 42
Moser C 6
Muller H 41
Mussel HH 20
Muta T 15
Myers TJ 17
Nadler LM 49
Nagata K 61
Nagura E 8
Nazerian K 63
Negoro S 37
Nussbaum-Blumen 9
O'Dorisio MS 22
O'Dorisio TM 22
Ogiu T 69
Ogura M 8
Oh SK 24
Oh WS 31
Ohtsuki Y 61
Onder O 17
Oscier DG 58
Ozer H 9
P'Eng FK 65
Paietta E 6

Parker JW ..... 18
Pastuszak WT ..... 17
Pinkus GS ..... 2
Price GB ..... 1
Pross HF ..... 19
Pykhtina AA ..... 54
Radaszkiewicz T ..... 6
Rader RL ..... 34
Ratliff TL ..... 66
Rebar L ..... 50
Reinherz EL ..... 46
Rickles FR ..... 17
Ritz J ..... 49
Roberts P ..... 58
Rosenfeld C ..... 57
Rossowski W ..... 36
Rouse BT ..... 25
Rubin P ..... 19
Russell RG ..... 25
Rytwinski K ..... 30
Said JW ..... 2
Saito O ..... 69
Saito T ..... 44
Sanger VL ..... 63
Saviotti F ..... 5
Sawada H ..... 11
Scheid MP ..... 38
Scheiner O ..... 20
Schlossman SF ..... 49
Schmitt M ..... 20
Schneiberg K ..... 30
Schwarzmeier JD ..... 6
Sebek B ..... 29
Seon BK ..... 37
Serrou B ..... 55
Serrou B ..... 57
Shah-Reddy I ..... 59
Sharma JM ..... 63
Sheibani K ..... 29
Shiraishi Y ..... 61
Simmler MC ..... 27
Siraganian RP ..... 53
Smith SD ..... 60
Soehnlen BJ ..... 14
Song SK ..... 31
Sparkes RS ..... 40
Stanley P ..... 14
Stanners CP ..... 1
Stass SA ..... 4
Staughton RC ..... 13
Steinmetz JC ..... 48
Stewart SS ..... 1
Sun L ..... 38
Suzuki H ..... 8
Takamatsu J ..... 8
Takei I ..... 44
Taniguchi M ..... 44
Taylor CR ..... 18
Thiel E ..... 12
Todd RF ..... 49
Tomioka H ..... 44
Trepinska E ..... 56
Tsang KY ..... 68
Tubbs R ..... 29
Tung TC ..... 32
Tura S ..... 5
Uchino H ..... 11
Ueda K ..... 11
Valenzuela R ..... 29
Vecek N ..... 64
Villemez CL ..... 47
Warchol JB ..... 36
Warnke RA ..... 10
Wasik R ..... 35
Watanabe E ..... 8
Watanabe T ..... 38
Wayner EA ..... 26
Webb PJ ..... 26
Weiss R ..... 29
Widmer MB ..... 67
Witter RL ..... 63
Wood GW ..... 60
Wybier-Franqui ..... 27
Yamada K ..... 8
Yamada Y ..... 15
Yamada Y ..... 62
Yamamura M ..... 8
Yasui E ..... 28
Yokomaku S ..... 8
Yoshimoto S ..... 3
Yoshimoto S ..... 61
Yoshizaki K ..... 37
Zahringer M ..... 52
Zarling JM ..... 43
Zola H ..... 7

# VIDEOTAPES

## ON CURRENT TOPICS IN CANCER RESEARCH

A pilot project of the International Cancer Research Data Bank (ICRDB) Program of the National Cancer Institute

*Three series are available . . .*

### THE RELATION OF CARCINOGEN ACTION ON DNA TO CELL TRANSFORMATION

| | | |
|---|---|---|
| PETER MAGEE<br>Fels Research Institute | *Keynote Address* | #VK01<br>28 min. |
| JAMES K. SELKIRK<br>Oak Ridge National Laboratories | *Metabolic Activation and Macromolecular Binding of Chemical Carcinogens* | #VK02<br>51 min. |
| PHILIP C. HANAWALT<br>Stanford University | *Cellular Responses to Damaged DNA* | #VK03<br>54 min. |
| CHARLES HEIDELBERGER<br>University of Southern California | *Mutagenesis and Oncogenic Transformation of Mouse Embryo Cells* | #VK04<br>54 min. |
| FRED RAPP<br>Milton S. Hershey Medical Center | *The Interaction of Herpesviruses and Host Cells Leading to Latency or Transformation* | #VK05<br>52 min. |
| | *Panel Discussion* | #VK06<br>31 min. |

### MECHANISMS OF METASTASIS

| | | |
|---|---|---|
| ISAIAH FIDLER<br>Frederick Cancer Research Center | *The Heterogeneous Nature of Cancer Metastasis and Implications for Therapy* | #VB01<br>47 min. |
| GEORGE POSTE<br>Smith, Kline and French Laboratories | *Phenotypic Analysis of Metastatic Cell Populations* | #VB02<br>42 min. |
| LANCE LIOTTA<br>National Cancer Institute | *Tumor Cell Invasion of Basement Membranes and Extracellular Matrices* | #VB03<br>33 min |
| EVERETT SUGARBAKER<br>Miami Cancer Institute | *Some Clinical Characteristics of Metastasis in Man* | #VB04<br>41 min. |

### AUTOMATED CYTOLOGY

| | |
|---|---|
| Part One: Principles and Techniques | #VB05<br>56 min. |
| Part Two: Biological Applications | #VB06<br>52 min. |

VIDEOTAPES ON CURRENT TOPICS IN CANCER RESEARCH are in the 3/4" U-matic format and can be played on video equipment which accepts the NTSC standard (the standard for videotapes produced in the U.S.).

The videotapes are available on a loan basis. If you would like to schedule viewing for your group, or for more information, please write to:

Cancer Information Dissemination and Analysis Center (CIDAC)
Franklin Research Center
20th and Benjamin Franklin Parkway
Philadelphia, PA 19103

Please specify three choices for viewing dates, and the tapes desired.

# More Than Just A Fancy Name

**Mention CANCERLINE to your librarian** and the world's foremost collection of cancer information is at your disposal. With the help of this computerized data system, you can obtain information on the following:

## Cancer Literature

The literature date base, **CANCERLIT**, allows you to survey more than 3,000 biomedical journals for information on your topic of interest. Your search will also alert you to meeting proceedings, monographs, and books published in that area. Informative abstracts averaging 200 words are provided with each citation;

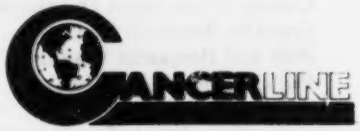
## Current Cancer Research

The data base **CANCERPROJ** allows you to retrieve descriptions of current work in any cancer research area. The descriptions, which state research objective, methodology, and experimental results, are supplied for projects underway in 77 countries around the world.

## Cancer Therapy Protocols

The **CLINPROT** section of CANCERLINE is designed primarily for clinicians. It provides detailed summaries of currently active experimental protocols for any cancer site, agent, or type.

**Ask your biomedical librarian about CANCERLINE.**
CANCERLINE is sponsored by the International Cancer Research Data Bank—a program of the National Cancer Institute.



# Keep Up with the Cancer Literature

## Each Month
## You Can Receive Abstracts
## Covering Your Specialty Area

- This convenient service — called Auto SDI* — is as near as your nearest biomedical library. Discuss your research interests with the librarian who will design an appropriate search strategy.
- Abstracts of the latest published literature are searched automatically each month and those related to your interests are delivered to you on a regular basis.
- The abstracts you receive are selected from more than 4,000 monthly entries made into CANCERLIT — the extensive cancer literature data base of the National Cancer Institute.

## Talk With Your Librarian
## About the Auto SDI Service TODAY.

*Auto SDI stands for Automatic Selective Dissemination of Information. It is a service provided to you, at minimal cost, by the International Cancer Research Data Bank (ICRDB) — a part of the National Cancer Institute.

**U.S. DEPARTMENT OF COMMERCE**
**National Technical Information Service**
5285 Port Royal Road
Springfield, Va. 22161

OFFICIAL BUSINESS

Penalty for Private Use, $300

**PRINTED MATTER**

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF COMMERCE
COM-211

THIRD CLASS
BULK RATE

U.S.MAIL

CB-17

**CANCERGRAMS** are distributed for the International Cancer Research Data Bank (ICRDB) by the National Technical Information Service (NTIS). **CANCERGRAMS** are available from NTIS on a standing order basis at $2 each for North American Continent addressees and $3 each for other addressees. An NTIS deposit account is required. For a list of subject categories or other information, please write to:

Subscription Section
National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161

**NOTICE OF MAILING CHANGE**

☐ Check here if you wish to discontinue receiving this publication.

☐ Check here if your address has changed and you wish to continue receiving this publication. (Be sure to furnish your complete address including zip code.)

Tear off cover with address label still affixed and send to:

Computer Support Center
ICRDB Program
IIT Research Institute
10 West 35th Street
Chicago IL. 60616

CB 17/82/06

NCI/ICRDB/CB17 82/06 PB82-931806

# ICRDB CANCERGRAM

# IMMUNOBIOLOGY AND CANCER

## Identification and Characterization of Immune Cells

SERIES CB17 No. 82/06 JUNE, 1982

This Cancergram is a service of the INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM of the U.S. National Cancer Institute. Every few weeks, an updated Cancergram containing abstracts of selected cancer-related articles recently published in more than 3000 journals, and dealing with the topic indicated by the above title, is sent to researchers working in this area. These researchers are identified on the basis of the description of their current research project that has been submitted to the ICRDB Program, directly or via granting agencies.

This Cancergram is prepared by the Cancer Information Dissemination and Analysis Center (CIDAC) for Virology, Immunology, and Biology. ***If this Cancergram is useful and valuable, please send your comments to the CIDAC address below, since future editions depend on user satisfaction and user needs:***

CIDAC FOR VIROLOGY, IMMUNOLOGY, AND BIOLOGY
SCIENCE INFORMATION SERVICES
FRANKLIN INSTITUTE RESEARCH LABORATORIES
20TH AND RACE STREETS
PHILADELPHIA, PA 19103

NEWARK PUBLIC LIBRARY
JUN 22 1982
U. S. GOVT. PUBS.
DEPOSITORY 376

SPECIAL ANNOUNCEMENTS FROM THE ICRDB PROGRAM WILL PERIODICALLY APPEAR AS FILLER PAGES IN THE BACK OF YOUR CANCERGRAMS. WATCH FOR THEM!

*In this issue:*


- CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS..... 1-10
- DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS..... 11-31
- LYMPHOCYTE AND DIFFERENTIATION ANTIGENS..... 32-44
- CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION..... 45-54
- EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS..... 55-65
- OTHER RELATED STUDIES..... 66-83


### CLASSIFICATION OF HUMAN LEUKEMIAS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service • National Institutes of Health • National Cancer Institute

HE 20.3173/2:

## AND LYMPHOMAS BY CELL SURFACE MARKERS

### 1. A THREE DIMENSIONAL ANALYSIS IF HUMAN PERIPHERAL BLOOD LEUKOCYTES WITH SCANNING ELECTRON MICROSCOPY: 2. A STUDY ON THE RELATIONSHIP BETWEEN SURFACE MARKERS AND SURFACE MORPHOLOGIES OF NEOPLASTIC CELLS FROM VARIOUS TYPES OF LYMPHOCYTIC LEUKEMIA.

**Kotani H**
**Second Div., Dept. Internal Medicine, Faculty Medicine, Kyoto Univ., Kyoto, Japan**
**Naika Hokan; 28(8):221-245 1981**

Immunologic and ultrastructural studies of cells from patients with T or B lymphoproliferative diseases (T-LPD and B-LPD, respectively) were conducted. Most cells from T-LPD patients r esembled normal T cells in having short, thin villi; the density of these villi varied in individual cases. Cells from patients with B-LPD were divided into five groups according to cell morphology and surface markers (SM). Analysis of clinical findings and SM suggests that neoplastic B-LPD cells resulted from monoclonal proliferation of cells in an arrested state of maturation. Different stages of maturation were indicated by variations in surface morphology ranging from smooth surfaces to 'stub-like', 'finger-like', and dense villi, ruffles, and blebs. Hairy cells (HC) resembled non-T cells from normal individual or patients with macroglobulinemia Waldenstrom; HC were marked by hairy projections and ruffles and by intracellular organelles similar to those found in two groups of B-LPD cells. These characteristics, together with the presence of an Ia-like surface antigen and the lack of phagocytic activity, suggested that hairy cells originated from lymphocytes. Neoplastic cells attached to marker RBC in the same manner as in normal rosettes, with broad attachment in E- and Fcgamma-rosettes and point attachment in Fcmu-rosettes. The number of surface receptors varied among subpopulations of both neoplastic and normal cells. (33 Refs) (In JPN)

### 2. MARKERS OF CELLULAR DIFFERENTIATION IN ACUTE LYMPHOBLASTIC LEUKEMIA.

**Peiper SC, Stass SA**
**Div. Pathology, St. Jude Children's Res. Hosp., 332 N Lauderdale, PO Box 318, Memphis, TN, 38101**
**Arch Pathol Lab Med; 106(1):3-8 1982**

Acute lymphoblastic leukemia (ALL) is a heterogeneous entity that can be subcategorized on the basis of morphologic aspects, immunologic markers, membrane antigens, and enzymatic content of the blast forms. Subgroups corresponding to T-cell, pre-T-cell, pre-B-cell, and non-T-, non-B-lymphocyte derivations can be defined by immunologic markers, and the biologic differences are supported by the differential expression of membrane antigens and of nuclear, lysosomal, cytoplasmic, and membrane enzymes. These studies ease the diagnosis and characterization of ALL and enhance understanding of this disease. (Author abstract) (81 Refs)

### 3. CHANGES IN LYMPHOCYTES AS AN EARLY SIGN OF RELAPSE IN ADULT ACUTE LEUKEMIA.

**Kawamura S, Abe I, Saitoh A, Yamaya T, Tsuchida S, Chiba Y, Yoshida Y**
**First Dept. Internal Medicine, Hirosaki Univ. Sch. Medicine, Hirosaki 036, Japan**
**Tohoku J Exp Med; 135(3):237-245 1981**

Laboratory tests were administered to 23 patients (17 males, 6 females; 18-53 yr old) during the remission phase of leukemia (15 acute myelocytic; 8 acute lymphocytic) until relapse occurred, and an attempt was made to correlate test result changes with the onset of relapse. Blood examinations consisted of total protein, albumin/globulin ratio, lactate dehydrogenase activity, zinc sulfate test, erythrocyte sedimentation rate, C-reactive protein, and immunoglobulin levels (IgG, IgA, IgM), determined once during remission and once during relapse. Red cell counts, white cell counts with differential hemoglobin levels, platelet counts, and reticulocyte counts in the peripheral blood were done every 2 wk after remission until relapse. T-cells and B-cells were counted by E-rosette and EAC-rosette formation; blastogenesis of lymphocytes was measured by 3H-uridine incorporation after stimulation with phytohemagglutinin-P. Bone marrow cells aspirated from the sternum and ilium were cultured. Neither laboratory blood tests nor blood counts showed significant changes in association with relapse. Bone marrow cultures did not show significant differences either, but percentages of both T- and B-cells had decreased markedly at the time of relapse. A decrease in T- and B-lymphocytes or an increase in peripheral blood lymphocytes greater than 40-50% during maintenance therapy indicates the need for immediate bone marrow puncture. (15 Refs)

### 4. ACID PHOSPHATASE STAINING PATTERN AS AN INDICATOR OF T-CELL ACUTE LEUKEMIA.

**Savage RA, Valenzuela R, Hoffman GC**
**Dept. Lab. Hematology, Cleveland Clinic Foundation, 9500 Euclid Ave., Cleveland, OH, 44106**
**Am J Clin Pathol; 76(6):760-764 1981**

Acid phosphatase staining pattern has been variably advocated and discouraged as an indicator of T-cell differentiation of acute lymphoblastic leukemias. This study indicates that acid phosphatase staining pattern will correlate with the results of E rosette testing in both T-cell and non-T, non-B acute lymphoblastic leukemias in over 90% of cases. Acid phosphatase staining pattern may reliably be used to indicate T-cell differentiation in acute lymphoblastic leukemia in cases where insufficient material for E rosette testing is available. (Author abstract) (10 Refs)

### 5. CLINCO-MORPHOLOGICAL CLASSIFICATION OF ACUTE LEUKEMIAS.

**Maldonado J, Ramirez G, Artacho MC**
**Servicio de Hematologia y Hemoterapia, C.S. 'Carlos Haya' de la S.S., Malaga, Spain**
**Sangre (Barc); 26(5C):946-962 1981**

The important advances attained in the last 10 yr on the acute leukemia cell have introduced striking modifications in the classification of, and subsequently the therapeutical strategy for, this disease. This cytomorphological classification proposed by WHO in 1973 has been displaced by that devised in 1976 by the FAB cooperative group. Modifications to the FAB proposal concerning both myeloid and lymphocytic leukemias have emerged in 1980 and 1981 with the assistance of cytochemical techniques. The new criteria have been applied by the authors to fifty cases of each acute leukemia variety in order to establish base-line comparisons. Histological bone-marrow studies, electron microscopy, and automation of blood differential count are diagnostic tools to be applied in the classification of leukemic cells . Cytogenetics, cell-culture techniques, and cell kinetics are further paths to follow in acute leukemia identification. However, the most striking progress in this field comes from the discovery of cell membrane- and enzyme-markers, giving rise to a new immunologic classification of

acute lymphoblastic leukemia. The clinical profile of acute leukemia represents a landmark in the classifications when prognostic purposes are sought, so finding the possible correlations between all study methods is one of the aims of the present report: in this connection, the existing protocols have been applied by the authors to one-hundred patients of each leukemia variety. The special forms of acute leukemia are finally considered on the bases of the diagnostic advances commented above, in an attempt to re-evaluate such forms. This review was made as an introduction to the round-table conference in which other contributors will undoubtedly focus their attention on the topics concerning acute leukemia. (Author abstract) (40 Refs) (In SPA)

## 6. ANALYSIS OF THE PEANUT AGGLUTININ-BINDING SITE AS A DIFFERENTIATION MARKER OF NORMAL AND MALIGNANT HUMAN LYMPHOID CELLS.

**Galili U, Galili N, Or R, Polliack A**
**Dept. Haematology, Hadassah Univ. Hosp., Jerusalem, Israel**
**Clin Exp Immunol; 43(2):311-318 1981**

Human lymphoid cells obtained from bone marrow, thymus, spleen, and lymph node tissues were studied for their capacity to bind fluorescein-bound (FITC) peanut agglutinin (PNA). The PNA-binding capacity of a variety of leukemic and cultured human lymphoblastoid cells was examined to determine if this membrane characteristic can be used to distinguish subsets of leukemic cells. Of normal cells from lymphoid organs studied, only thymocytes bound PNA. Peripheral blood lymphocytes did not bind PNA. RBC E-rosetting thymocytes bound PNA, whereas prothymocytes that did not form E rosettes did not bind PNA. Fetal splenic lymphocytes, like their adult counterparts, lacked PNA-binding capacity. Lymphoblastoid cell lines were examined for staining with FITC PNA. The only T-derived line that exhibited strong PNA binding was acute lymphoblastic leukemia (ALL)-derived Be13 cells; Hodgkin's disease-derived HD-MAR cells that readily form E rosettes interacted very weakly with PNA. Other T lines that express human T antigen lacked PNA-binding ability. All B cell-derived cell lines originating from African or American type Burkitt lymphoma exhibited strong specific binding of FITC-PNA. Other B-cell lines also exhibited PNA binding. Leukemic cells from 3/15 ALL patients, 3/3 with non-Hodgkin's lymphoma, and 1/1 with hairy cell leukemia exhibited PNA binding. Cells from 3/11 acute myeloid leukemia patients showed partial PNA binding. No leukemic cells from patients with chronic lymphocytic (9 patients) or chronic myeloid (4) leukemia bound FITC PNA. The usefulness of PNA as a differentiation marker in malignant cells is discussed. (31 Refs)

## 7. CLINICAL, HEMATOLOGICAL AND PATHOLOGICAL FEATURES OF T-CELL LEUKEMIA-LYMPHOMA IN THE NAGASAKI DISTRICT.

**Kinoshita K, Kamihira S, Yamada Y, Amagasaki T, Ikeda S**
**Dept. Hematology, Atomic Disease Inst., Nagasaki Univ. Sch. Medicine, Nagasaki, Japan**
**Nippon Ketsueki Gakkai Zasshi; 44(7):1431-1443 1981**

Surface natures of malignant cells from lymph nodes and the peripheral blood of 140 patients with non-Hodgkin's lymphoma (NHL) in the Nagasaki district were examined for T and B cell characteristics. Surprisingly, 110 cases (78.6%) were of the T-cell form on the basis of spontaneous rosette formation with sheep erythrocytes. Of the remaining cases, 17 were B-cell origin (monoclonal S-Ig positive), 9 were non T-, non B-cell and 4 cases were undetermined. Seventy-one (65.4%) of the T-cell lymphomas were of leukemic form, characterized by pleomorphism in the peripheral blood cell size, and histological appearance. However, most of the leukemic T-cells showed obvious lymphocytic differentiation, with condensed nuclear chromatin and scant cytoplasm, although in many of the cases, lymphomatous infiltrate was dominated by either pleomorphic lymphoid cells or medium-sized cells, accompanied by occasional large multinucleated lymphoid cells. Clinically, they primarily involved middle-aged and elderly subjects, and were characterized by wide spread organ invasion (particularly to the liver, spleen and skin), susceptibility to various infections, complication of hypercalcemia and a poor prognosis. A mediastinal mass was not observed in all cases. The patients had a median survival of only 7.5 mo. On the other hand, non-leukemic T-cell lymphomas, half of which histologically showed the monotonous infiltrates of large lymphoid cells, were not different in any way from usual manifestation of malignant lymphoma with massive lymphadenopathy. These patients were generally resistant to chemotherapy and many of them died of the progression of the lymphoma within almost 1 yr. On the basis of surface marker, cell morphology, cytochemistry, and DNA synthesis of the malignant, pleomorphic T-cells, it was suggested that large lymphoid cells, namely, T-immunoblast differentiated to mature lymphocytes, resulting in a pleomorphism of the lymphoid infiltrates and leukemic manifestation. (Author abstract) (32 Refs)

## 8. CELL MARKERS IN HAIRY CELL LEUKEMIA STUDIED IN CELLS FROM 51 PATIENTS.

**Jansen J, Schuit HR, Meijer CJ, Van Nieuwkoop JA, Hijmans W**
**Isolation Ward, Building 16, Leiden Univ. Medical Center, Building 16, 2333 AA Leiden, The Netherlands**
**Blood; 59(1):52-60 1982**

To determine the maturation arrest of the neoplastic cells of hairy-cell leukemia (HCL) and the spectrum of the surface markers on these cells, a series of 51 patients with this disease wa s studied. The cells of all but two of the patients showed monoclonal surface Ig with respect to light chains. In about one-third of the cases, only gamma heavy chain determinants were present on the cells; the majority carried multiple heavy chain determinants as documented by the application of different fluorochromes. Two patients each showed two different clones of cells, both of the same light chain type. In one of these two patients, two paraproteins were present in the serum. Intracytoplasmic Ig was found in only 4 of 39 cases, in all instances being IgM. All cases studied concerned cells with FcIgG receptors; however, the density of this receptor varied. FcIgM receptors also showed a spectrum of density, with some cases showing very few FcIgM-positive cells. Receptors for C3 were not observed on the hairy cells. Serum immunoglobulin levels were normal or increased. Paraproteins were found in the sera of 4 of 38 patients. These data suggest that HCL is a neoplasm of B lymphocytes. The neoplastic cells are probably arrested at a more mature stage than the cells of chronic lymphocytic leukemia. The multiple isotypes on the cells indicate a block at the 'switch' phase from the small mu-carrying lymphocyte to the larger Ig-producing lymphocyte or plasma cell. (Author abstract) (42 Refs)

### 9. MEMBRANE MARKERS, TDT AND ULTRASTRUCTURAL CYTOCHEMISTRY IN APPARENTLY NON MYELOID LEUKEMIAS (MEETING ABSTRACT).

Zittoun R, Marie JP, Perrot JY, Zittoun J, Boucheix C, Rosenfeld C
Service d'Hematologie de l'Hotel Dieu Paris, Paris, France
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

A prospective study including the determination of the common acute lymphoblastic antigen (CALLA), the human T lymphocyte antigen (HUTLA), the terminal deoxynucleotidyl transferase (TdT) and the ultrastructural detection of peroxidase activity (POEM) was performed on 16 apparently non myeloid, non T non B acute leukemias. These patients were selected from 73 adult leukemic patients by the negativity of their routine cytochemical myeloid markers (myeloperoxidase, Sudan Black B, chloracetate activity), and the absence of B (surface IG) or T (spontaneous sheep (SRBC rosettes) markers. The anti CALLA serum was prepared by rabbit's immunization against Reh cell line. The TdT assay was measured using the biochemical method of Bollum modified by Hoffbrand et al. The detection of POEM was performed according to the techniques of Breton-Gorius et al. After this multiparametric study, all leukemias could be classified as following: 6 CALL (CALLA+), 1 pre-T ALL (CALLA+, HUTLA+), 2 poorly differentiated ALL (CALLA-, POEM-, TdT+), 5 poorly differentiated AML (CALLA-, POEM+), and 2 mixed leukemias (CALLA+, POEM+). The cytogenetic studies has shown that 2 of the CALL, 3 of the AML and the two mixed leukemias were Ph 1+. We conclude that POEM detection is useful to classify the apparently non myeloid leukemias with negative immunological markers. (no Refs)

### 10. OCULAR ADNEXAL LYMPHOID TUMORS: CORRELATIVE ULTRASTRUCTURAL AND IMMUNOLOGIC MARKER STUDIES.

Jakobiec FA, Iwamoto T, Knowles DM
Manhattan Eye, Ear, and Throat Hosp., 210 E 64th St., New York, NY, 10021
Arch Ophthalmol; 100(1):84-98 1982

Twenty-two ocular adnexal lymphoid infiltrates were analyzed by electron microscopy as well as immunologically and cytochemically. Five reactive polyclonal lesions were found to be preponderantly composed of small mature lymphocytes (presumably T cells) with clumped nuclear chromatin, sparse cytoplasmic organelles, and numerous monoribosomes. In 11 monoclonal B-cell lesions, both the 1-um plastic sections examined by light microscopy and the electron micrographs disclosed immature cells, with more dispersed nuclear chromatin, prominent nucleoli, abundant cytoplasmic polyribosomes, and increased numbers of mitochondria and strands of endoplasmic reticulum (particularly in plasmacytoid lesions). The remaining six monoclonal B-cell lesions were composed of comparatively well-differentiated cells requiring electron microscopy to show somewhat more prominent nucleoli, slightly less dense clumping of the nuclear chromatin, increased numbers of mitochondria and short segments of rough-surfaced endoplasmic reticulum, and monoribosomes rather than polyribosomes. The importance of distinguishing this group of well-differentiated monoclonal lesions from the less well-differentiated ones was underscored by the results of the follow-up examinations, in that no evidence of extraorbital disease has been discovered in the former group, while a 50% incidence occurred in the latter. (Author abstract) (37 Refs)

## DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS

### 11. STUDY OF ASIALOGANGLIOSIDES ON SURFACE MEMBRANES OF RAT BONE MARROW CELLS AND MACROPHAGES.

Taki T, Tadagi K, Kamada R, Matsumoto M, Kojima K
(c/o Matsumoto) Dept. Biochemistry, Shizuoka Coll. Pharmacy, Oshika, Shizuoka, Shizuoka 422, Japan
J Biochem (Tokyo); 90(6):1653-1660 1981

The presence of asialogangliosides on membrane surfaces of rat bone marrow cells and macrophages was studied by an immunological method using anti-glycolipid antibodies with high specificity. The antibodies against N-acetylgalactosaminyl(beta1-4)galactosyl(beta1-4) glucosylceramide (GA2), galactosyl(beta1-3)N-acetylgalactosaminyl-(beta1 4)galactosyl(beta1-4) glucosylceramide (GA1) and fucosyl(alpha1-2)galactosyl(beta1-3)N acetylgalactosaminyl(beta1-4) galactosyl(beta1-4)glucosylceramide (Fuco-GA1) were prepared, and used for cytotoxicity testing and indirect staining by the immunofluorescence technique. In the cytotoxicity test, approximately 40-50% of rat intraperitoneal macrophages were killed by each of the anti-glycolipid antisera. This finding was confirmed by the indirect immunofluorescence staining method with the purified anti-GA2, anti-GA1 and also anti-Fuco-GA1 IgG. When a rat was preimmunized with bovine serum albumin, all macrophages induced in ascites fluid were found to possess GA1 by the staining method. Immature granulocytes were stained specifically with the anti-GA2 antibody. Granulocytes, myelocytes, and megakaryocytes were stained with the anti-GA1 antibody. Blastic myelocytes were stained with the anti-Fuco-GA1 IgG, but lymphocytes were not stained with any of these anti-asialoganglioside antibodies. From these observations, free-type cells such as macrophages and bone marrow cells were found to possess asialogangliosides as membrane components. (Author abstract) (28 Refs)

### 12. ACTIVATION OF FC RECEPTOR-BEARING LYMPHOCYTES BY IMMUNE COMPLEXES. II. KILLER LYMPHOCYTES MEDIATE FC LIGAND-INDUCED LYMPHOKINE PRODUCTION.

Neville ME, Lischner HW
Dept. Pediatrics, Temple Univ. Sch. Medicine, Philadelphia, PA, 19133
J Exp Med; 154(6):1868-1880 1981

The roles of the constant fragment (Fc) portion of IgG (Fc gamma) and of the Fc gamma receptors (FcR) in immune complex-induced lymphokine production (ICLP) were studied. Nonadherent lymphocytes enriched 3-to 4-fold in killer (K) cells and in other Fc gamma-binding cells showed antibody-dependent cellular cytotoxicity (ADCC) at approx 1/10 of the lymphocyte:target ratios required for unfractionated nonadherent lymphocytes. These K-cell enriched lymphocytes were induced by chicken antibody-sensitized RBC (EA), by aggregated human gamma globulin (AgHGG), or by sensitized P815 mouse mastocytoma cells to produce lymphocyte migration-inhibiting factor (LIF) at approx 1/10 of the concentration necessary for production of similar levels of activity by unfractionated cells. K cell but not natural killer (NK) cell depletion virtually eliminated ADCC and ICLP. K cells incubated with antibody-sensitized glutaraldehyde-treated P815 cells produced high levels of LIF in the supernatant; NK cells yielded little or no LIF activity when incubated with or without AgHGG. Iso-

lated Fc gamma fragments stimulated nonadherent lymphocytes to produce high levels of LIF activity. Fc gamma fragments did not inhibit WBC migration but blocked EA-rosette formation by lymphocytes. Binding of Fc gamma ligands to FcR of the appropriate lymphocytes was the only requirement for ICLP. (49 Refs)

### 13. MODULATION OF NATURAL CYTOTOXICITY BY ALLOANTIBODIES. V. THE MECHANISM OF A SELECTIVE AUGMENTING EFFECT OF ANTI-H-2 ANTISERA ON THE NATURAL KILLER ACTIVITY OF MOUSE SPLEEN CELLS.

**Saxena RK, Saxena QB, Adler WH**
**Clinical Immunology Section, Gerontology Res. Center, NIA, NIH, Baltimore, MD, 21224**
**Cell Immunol; 65(1):115-130 1981**

Treatment of mouse spleen cells with specific anti-H-2 antisera augments their natural killer (NK) activity against K562 cells but not against YAC target tumor cells. The same population of natural killer cells was found to lyse K562 as well as YAC target cells, since (a) depletion of YAC reactive NK cells by absorption on YAC monolayers resulted in a concomitant depletion of anti-K562 NK activity of mouse spleen cells, and (b) both K562 and YAC cells could inhibit their own as well as each others lysis in a cross-competition assay. Anti-H-2 antiserum could not induce anti-K562 NK activity in spleen cells previously depleted of NK cells by absorption on YAC monolayers, indicating that alloantiserum does not act by recruiting otherwise nonreactive cells to become cytotoxic toward K562 target cells. In a target-binding assay, K562 binding of NK cells (T-cell, B-cell-, and macrophage-depleted spleen cells) increased five- to eightfold in the presence of anti-H-2 antiserum whereas YAC cells binding of NK cells was not increased. H-2 antigens per se did not appear to be involved in the alloantisera effect since anti-NK antiserum directed against a non-H-2 antigen selectively expressed on NK cells, showed a similar selective NK enhancing effect. Protein A, a reagent which binds to the Fc region of immunoglobulin molecules, completely blocked the alloantiserum induced augmentation of anti-K562 NK activity, but did not alter basal NK activity. Moreover, the F(ab)2 fraction of alloantibodies failed to enhance anti-K562 cytotoxic activity of mouse spleen cells, indicating a crucial role for the Fc portion of the alloantibodies attached to the NK cells, in NK augmentation. Utilization of several target cell lines with or without membrane Fc receptors (FcR) revealed that alloantiserum enhanced the lysis of only FcR+ target cells. It is proposed that alloantibody-coated NK cells, as a result of a secondary interaction between attached alloantibody and Fc receptors on target cells, interact more readily with the target cells and thereby cause a higher level of lytic activity. (Author abstract) (25 Refs)

### 14. CHARACTERIZATION OF E-ROSETTE-POSITIVE FC-RECEPTOR-BEARING CELLS BY FLOW CYTOMETRY.

**Froelich CJ, Bankhurst AD, Warner NL**
**Dept. Medicine and Pathology, Univ. New Mexico Sch. Medicine, Albuquerque, NM, 87131**
**Clin Immunol Immunopathol; 22(1):105-117 1982**

A subpopulation of human peripheral blood mononuclear cells which have the capacity to form spontaneous rosettes with sheep erythrocytes (E+) have been observed to also express a receptor for the Fc portion of immune complexed IgG. In this study quantitative flow cytometry is used to investigate the binding of human IgG to human E+ cells and to determine the relationship of these IgG-binding cells to the subsets of cells defined by OKT3 and OKM1 monoclonal antibodies. It was observed that a number of E+ cells bear an Fc receptor for monomeric human IgG; that all subclasses of IgG can bind to this subpopulation; that this subset overlaps with the T cell identified with rosetting techniques; and that virtually all of these E+ Fc receptor-positive cells binding monomeric IgG are phenotypically OKM1+ and OKT3-. (Author abstract) (19 Refs)

### 15. DESCRIPTION OF A SIMPLE, SPECIFIC, AND SENSITIVE TEST FOR THE DETECTION OF DETERGENT-SOLUBILIZED C3B RECEPTOR.

**Dierich MP, Ehlen T, Mussel HH**
**Institut fur Medizinische Mikrobiologie, Johannes-Gutenberg-Universitat, Hochhaus am Augustasplatz, 6500 Mainz, W. Germany**
**Immunobiology; 160(2):241-247 1981**

The C3b receptor was isolated from detergent-solubilized human erythrocyte membranes by a previously described technique. The receptor glycoprotein was shown to enhance EAC14oxy23b rosette formation with Raji lymphoblastoid cells. This provided a specific and sensitive test to detect the solubilized C3b receptor either in crude or highly purified form. The property of the C3b receptor tested by this assay appears to be analogous to properties of beta1H. (Author abstract) (12 Refs)

### 16. INHIBITION OF MONOCYTE COMPLEMENT RECEPTOR ENHANCEMENT BY LOW MOLECULAR WEIGHT MATERIAL FROM HUMAN LUNG CANCERS.

**Gless EJ, Abell CA, Kay AB**
**(c/o Kay) Dept. Clinical Immunology, Cardiothoracic Inst., Fulham Road, London SW3 6HP, England**
**Clin Exp Immunol; 43(3):540-548 1981**

We have studied the effect of dialysates from lung cancer homogenates to alter both the expression of complement (C3b) receptors per se and also to inhibit leucoattractant-induced enhancement of complement rosettes on monocytes from healthy individuals. Enhancement and enhancement-inhibition by tumor extracts were compared with material derived from normal lung excised some distance from the tumor. There was no significant difference between tumor homogenate (TH) and normal lung homogenate (NLH) in terms of enhancement of complement rosettes per se. In contrast, TH produced a dose- and time-dependent inhibition of leucoattractant-induced enhancement of C3b rosettes which was significantly different from that obtained with NLH. This enhancement-inhibition was observed with four undifferentiated, four squamous and three adenocarcinomas of lung. The degree of enhancement-inhibition was not related to the type of tumor or varying accompanying histological features such as necrosis and the degree of infiltration with inflammatory cells. Following gel filtration on Sephadex G-50 each type of cancer gave a major peak of inhibitory activity which eluted with molecules having an apparent molecular size of approx 3,000 daltons. A second larger peak (8,000-10,000 daltons) was also detectable with extracts from the undifferentiated and adenocarcinomas. These results support previous findings, mainly from experimental animals, indicating that 'anti-macrophage/monocyte principles' are elaborated from certain tumor types. (Author abstract) (20 Refs)

## 17. MAXIMIZING DIFFERENCES IN THE CONCANAVALIN A-INDUCED BLASTOGENIC RESPONSES OF LYMPHOCYTES FROM BREAST CANCER PATIENTS AND CONTROLS BY THE USE OF ALPHA-METHYL-D-MANNOSIDE.

Distasio JA, Cheresh DA, Schilder RJ, Vogel CL, Silverman MA, Lopez DM
Dept. Microbiology D4-4, Univ. Miami Sch. Medicine, P.O. Box 016960, Miami, FL, 33101
JNCI; 68(1):69-74 1982

In an attempt to magnify differences in the immune responses of potentially immunosuppressed cancer patients and normal controls, an assessment was made on the effects of the competitive inhibitor alpha-methyl-D-mannoside on the concanavalin A (Con A)-induced blastogenic responses of lymphocytes from each of these populations. Lymphocytes from breast cancer patients with metastatic disease were significantly deficient in their capability to undergo blast transformation regardless of whether the monosaccharide inhibitor was added to the assay cultures. In contrast, lymphocytes from breast cancer patients who did not display metastatic disease were capable of normal blastogenic responses to Con A. The addition of alpha-methyl-D-mannoside to lymphocyte cultures caused a significantly greater inhibition of the blastogenic responses of these patients' cells as compared to cells of normal controls. Thus the monosaccharide seems to serve as a useful reagent for optimizing differences between lymphocyte blastogenic responses of normal donors and those of immunodepressed donors. The results suggest that lymphocytes from breast cancer patients without clinically evident metastases possess some modification of their cell membrane. One possibility discussed was that the number or distribution of receptors for Con A on the membrane of lymphocytes of these patients is deficient. (Author abstract) (27 Refs)

## 18. ON THE DYNAMICS OF ABRIN BINDING TO RECEPTOR SITES IN NORMAL AND EPSTEIN BARR VIRUS TRANSFORMED LYMPHOCYTE CELL CULTURES.

Witten M, Bennett CE, Glassman AB, Gordon I
Dept. Mathematics, Univ. California, Santa Barbara, CA, 93103
J Recept Res; 2(2):175-201 1981

The effects of treatment with varying doses of abrin, a toxic D-galactose binding lectin, on DNA protein and synthesis of normal and Epstein Barr Virus (EBV)-transformed lymphocytes were investigated. Activation, stimulation, and relative toxicity factor indices were studied. Possible relationship between DNA and protein synthesis rates measured by simultaneous tritiated thymidine (3H-TdR) and (14C)leucine uptake were also studied. Receptor sites were determined with the use of 125I-abrin. Three repeated cell counts were made for each cell type, for each dose and time pair, and for each cell density and metabolic pair. Abrin is a metabolic toxin for the EBV-lymphocyte population and has also some effect on th e normal cell population. The EBV-transformed lymphocyte population is heterogeneous with three major lymphocyte subpopulations, each with a different number of receptor binding sites for abrin. Assuming that the size of the abrin receptor site is a fixed constant across the different morphological subpopulations, then the number of sites capable of being packed on the cell surface is a function of the cell surface area. The mean number of receptors bound/EBV-lymphocyte exerting biological influence is in the interval 59,264-370,040 receptors/cell. Theoretical and experimental results showed a significant resemblance. (16 Refs)

## 19. CAMP RECEPTOR PROTEINS AND PROTEIN KINASES IN HUMAN LYMPHOCYTES: FUNDAMENTAL ALTERATIONS IN CHRONIC LYMPHOCYTIC LEUKEMIA CELLS.

Weber W, Schwoch G, Wielckens K, Gartemann A, Hilz H
Physiologisch-Chemisches Institut, der Universitat Hamburg, Universitats-Krankenhaus Eppendorf, Martinistrabe 52, D-2000 Hamburg 20, W. Germany
Eur J Biochem; 120(3):585-592 1981

To study the significance of cAMP receptor proteins and protein kinase activities in tumor dys-differentiation, peripheral blood lymphocytes from normal donors and from patients with chronic lymphocytic leukemia were isolated by Percoll gradient centrifugation, and analyzed. Both normal and tumor lymphocyte populations were devoid of cell proliferation. Normal human lymphocytes contained about equal activities of histone kinase and 'casein kinase'. The tumor lymphocytes, however, exhibited drastically reduced values of all three protein kinase activities, the most pronounced decrease being observed with the 'casein kinase'. Total high-affinity cAMP-binding sites (= regulatory subunits R of cAMP-dependent protein kinases Type I and II) in leukemic lymphocytes were also strongly reduced. The findings in lymphocytes of chronic lymphocytic leukemia cannot be explained by the fact that they are B-type lymphocytes. Control experiments revealed that normal B cells do not differ significantly from total blood lymphocytes with respect to the parameters mentioned above. Biochemical correlates of the dys-differentiated status of these non-proliferating cells from patients with chronic lymphocytic leukemia, then, are represented by reduced levels of protein kinases, of basal cAMP as well as by changes in the R-protein pattern. The data indicate that both protein kinases Type I and Type II may relate to the state of differentiation, independently from cell proliferation. (57 Refs)

## 20. HIGH AFFINITY BINDING SITES ON PLASMA MEMBRANE OBTAINED FROM THE LYMPHOBLASTOID CULTURED 1301 CELL LINE FOR HIGHLY RADIOACTIVE SERUM THYMIC FACTOR.

Gastinel LN, Pleau JM, Dardenne M, Sasaki A, Bricas E, Morgat JL, Bach JF
INSERM U 25, Hopital Necker, 161 rue de Sevres, 75015 Paris, France
Biochim Biophys Acta; 684(1):117-126 1982

The interaction of the synthetic serum thymic factor (FTS, facteur thymique serique) with a plasma membrane preparation of human T lymphocytes from the lymphoblastoid T cell line 1301 was studied using 3H-labelled FTS (specific activity 120 Ci/mmol). The binding is temperature dependent and function of the concentration of both 3H-labelled FTS and membrane proteins. At 37 C, using 1 nM of 3H-labelled FTS a steady state is observed within 80 min. The binding is reversible, specific and saturable. Scatchard analysis reveals the existence of at least two binding sites with respective Kd of the order of 0.516 +-0.2 nM and 110 +-27.8 nM with concentrations of 0.186 +-0.045 pmol and 2.026 +-0.367 pmol per mg of membrane protein. (Author abstract) (36 Refs)

## 21. ENUMERATION OF LYMPHOCYTES AND THEIR SUBPOPULATIONS IDENTIFIED BY BACTERIAL ADHERENCE IN BLOOD SMEARS OF PATIENTS WITH BREAST TUMORS.

Felix E, Katz S, Teodorescu A, Teodorescu M
(c/o M. Teodorescu) Dept. Microbiology and Immunology, Univ. Illinois Medical Center, Chicago, IL, 60612
J Surg Oncol; 18(4):323-329 1981

Peripheral blood lymphocyte counts were determined in 57 breast clinic patients. These patients were grouped into four clinical/pathological groups: 18 had benign breast disease, 13 had a history of breast cancer but were free of disease at the time of the study, 7 had a history of breast cancer and were free of disease at the time of the study but were on adjuvant chemotherapy, and 19 had active metastatic breast cancer. Two parameters were investigated in a double blind study: (1) the absolute lymphocyte counts and (2) the percentages of lymphocytes that bound different bacteria as markers of lymphocyte subpopulations in conventionally stained blood smears. A significant reduction in mean lymphocyte counts was demonstrated in patients with advanced disease. A significant increase in these counts was found in patients who were free of disease following surgical treatment alone. The T1 T2 cells (our denomination), the subpopulation of cells responsible for specific killing in vitro and for suppression of natural cytotoxic cells, was significantly reduced in patients with advanced disease under treatment. The T/B cell ratio in all groups was the same and within normal range. These observations suggest that the observed decrease in the total lymphocytes is due not only to an overall decrease in all classes of lymphocytes but especially in those responsible for specific cell-mediated reactions. They also show that bacteria can be used as reliable reagents for the identification of lymphocyte subpopulations in blood smears. (Author abstract) (21 Refs)

## 22. TTHETA-AND TGAMMA-CELL SUBSETS IN NORMAL AND LEUKEMIC CATTLE.

Surovas V, Pieskus J, Tamosiunas V, Sadauskas P
Inst. Biochemistry, Acad. Sciences Lithuanian S.S.R., 232021 Vilnius, Mokslininkų 12, USSR
Thymus; 4(1):31-43 1982

T-cell subsets in the blood and lymphoid organs of normal and chronic lymphocytic leukemic cattle were examined; the T-cells bore receptors for IgM (Tmu) and IgG (Tgamma). Bovine Tgamma cells were more susceptible to the leukemic process than Tmu cells, acquiring enhanced adhesive properties during the process. (32 Refs)

## 23. STUDIES OF T AND B LYMPHOCYTES IN GYNECOLOGICAL MALIGNANCIES.

Sun Y, Li C, Zhang G, Kuang Y
Women's Hosp., Shanghai First Medical Coll., Shanghai, People's Republic of China
Zhonghua Fuchanke Zazhi; 16(2):93-96 1981

Lowered cellular immunity is often observed in cancer patients, which was related to their clinical conditions and prognosis. Immunological findings are described for 22 cases (34-74 yr old) of gynecologic malignancies, consisting of 12 cases of cervix carcinoma, 5 of uterine carcinoma, 3 of ovarian carcinoma, 1 of uterine sarcoma and 1 of choriocarcinoma. The majority of patients have not undergone treatment. Based on immunological examination of peripheral B- and T-lymphocytes and skin tests using old tuberculin, streptokinase-streptodornase and phytohemagglutinins, the cellular immunity in malignant gynecologic tumors was inhibited, with positive skin reaction, total T-lymphocyte count and active E-rosette formation markedly lower than those of controls. The percentage of lymphocytes and the absolute values of E-rosettes were related to the pathological stage of the tumor. The value of using E-rosettes in the immunologic evaluation of lymphocytes is discussed. (8 Refs) (In CHI)

## 24. ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY IN HUMAN CANCER: CHARACTERIZATION OF PATIENT LEUKOCYTE ACTIVITY AND TREATMENT EFFECTS.

Hersh EM, Murphy SG, Gutterman JU, Morgan J, Quesada J, Zander A, Stewart D
M. D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030
Cancer; 49(2):251-260 1982

Antibody-dependent cell-mediated cytotoxicity (ADCC), mediated by peripheral blood Hypaque-Ficoll separated mononuclear cells, was studied in humans using chicken erythrocytes (CRBC) incubated in a 1:1,200 dilution of rabbit anti-CRBC and human B erythrocytes (HRBC) incubated in a 1:20 dilution of isoantibody. At the optimal target effector ratio of 3:1, ADCC to both CRBC and HRBC was significantly higher than normal in 27 lung cancer, 18 malignant melanoma, and 7 colon cancer patients, but not in 20 breast cancer patients. Chemotherapy (single-agent or combination) in 12 patients did not affect ADCC in vitro but significantly suppressed ADCC to both targets after only 4 or 5 days of therapy in vivo (ADCC to CRBC, 47.4 to 24.1% lysis: ADCC to HRBC, 48.1 to 16.3% lysis). Immunotherapy with intravenous (IV) Corynebacterium parvum or IV methanol extraction residue of BCG (MER) boosted ADCC to both targets within 4 to 7 days of the first dose. It was found that ADCC to HRBC but not to CRBC was completely absent in three cases of active hairy cell leukemia but was present in two cases in remission. The ADCC to HRBC showed an age-dependent increase in both the 51 normal subject and the cancer patients. This was not observed for ADCC to CRBC. The ADCC to CRBC was mediated mainly by an Fc-receptor-positive, nonadherent, small lymphocyte, and ADCC to HRBC was mediated entirely by an adherent monocyte. The ADCC did not correlate significantly with the H3 thymidine incorporation of peripheral blood mononuclear cells, cultured without stimulation for either 1 or 7 days. It also did not correlate with the number of residual granulocytes in the mononuclear cell suspensions. Measurement of ADCC is a useful method of characterizing host defense in malignant disease and its modification by therapy. (Author abstract) (48 Refs)

## 25. PROGNOSTIC SIGNIFICANCE OF IMMUNOLOGICAL TESTS IN LUNG CANCER.

Check IJ, Hunter RL, Karrison T, DeMeester TR, Golomb HM, Vardiman J
Dept. Pathology and Lab. Medicine, Emory Univ. Sch. Medicine, Atlanta, GA, 30322
Clin Exp Immunol; 43(2):362-369 1981

The prognostic significance of several immunological parameters was studied in 94 cases of lung cancer. Blood samples were obtained from 71 patients with newly-diagnosed non-oat cell carcinoma (NOCC) prior to treatment (including 39 with squamous cell carcinoma, 27 with adenocarcinoma, and 5 with undifferentiated carcinoma) and from 23 patients with unresectable bronchogenic NOCC that had been treated prior to the study. Parameters measured included percentage of lymphocytes in gradient-derived cell suspension (%LG), WBC count,

lymphocyte (LC) count, percentage of E-rosette formation (ERF) at 4 C or 37 C, response to pokeweed mitogen (PWM), and response to concanavalin A (Con A). The greatest significance was shown by %LG, which decreased with advancing disease stage. WBC and LC counts and ERF showed no significant change. PWM response decreased significantly and Con A decreased insignificantly; analysis of results of test pairing suggested that PWM and Con A responses are dependent on %LG. The prognostic value of %LG was significant for the total number of patients and for those within a given stage. Median survival times (MST) for patients with resectable tumors were well beyond 12 mo for those with 60%LG and 12 mo for those with 40%LG. MST for patients with unresectable tumors were 5.5 mo for those with 60% LG and 4.2 mo for those with 40% LG. Analysis of cell buoyant density indicated that decreased %LG resulted from decreased density of nonlymphoid cells. Measurement of %LG was confirmed as a simple prognostic indicator. (39 Refs)

## 26. CELL-MEDIATED IMMUNITY IN BREAST CANCER PATIENTS IN RELATION TO CLINICAL STAGES.

**Pasqualini RS, Giraudo Conesa LC, Lynch M, Sardi J, Pujato D**

**Instituto de Investigaciones Hematologicas, Academia Nacional de Medicina, Melo 3081, (1425) Buenos Aires, Argentina**

**Cell Mol Biol; 27(5):551-556 1981**

Cell-mediated immunity of patients with breast cancer at clinical stage I, II, III or IV, prior to any therapy, was evaluated in relation to their clinical stage. In vitro peripheral blood studies included: absolute number of lymphocytes/ul; absolute number of T-lymphocytes/ul (E-rosette-forming cells); lymphocytes' response to phytohemagglutinin. In vivo assays consisted of delayed hypersensitivity skin tests to ubiquitous antigens and 2,4-dinitrochlorobenzene sensitization. The results obtained can be summarized as follows: absolute numbers of total lymphocytes/ul were lower in breast cancer patients than in the normal group. However, the values corresponding to Stage IV were the only ones significantly different when compared with normal and with any other clinical stage. Absolute numbers of T-lymphocytes/ul were lower in breast cancer patients than in the normal group, and statistically significant differences were found when Stages II, III or IV were each compared with the normal group. Furthermore, a significant decrease in the number of T-lymphocytes was observed in Stage IV, as compared with any other clinical stage. Transformation indices obtained from lymphocyte cultures of patients were lower than those observed in normals. However, the values corresponding to Stage I were the only ones significantly different. Moreover, the transformation index of Stage I was also significantly lower than that of Stage IV. The percentages of positive skin tests to purified protein derivative were significantly lower in Stage II, III or IV than in either Stage I or the normal group. The percentage of positive skin tests to Candida albicans antigen was significantly decreased in Stage IV. Finally, the percentages of positivity to 2,4-dinitrochlorobenzene sensitization were lower in all clinical stages of breast cancer than in the normal group. In Stage II, immune competence was not affected by metastatic involvement of regional lymph nodes. The observed differences cannot be attributed to age. (Author abstract) (27 Refs)

## 27. CONTRASTING PATTERNS OF PROTEIN KINASE ACTIVITIES AMONG NORMAL PERIPHERAL BLOOD LYMPHOCYTE SUBPOPULATIONS AND LYMPHOID CELL LINES.

**Elias L, Longmire J, Bankhurst AD**

**Cancer Res. and Treatment Center, University New Mexico, Albuquerque, New Mexico, 87113**

**J Lab Clin Med; 99(1):56-63 1982**

Human peripheral mononuclear cell suspensions were separated into E-rosette-positive (T cell) and E-rosette-negative (non-T cell) fractions and assayed for cAMP binding activity and histone and casein kinase activity, in the presence and absence of cAMP. Each of these activities was higher in E-rosette-positive than E-rosette-negative fractions. Cyclic AMP binding and histone kinase activities w ere further noted to be higher in T lymphoblastoid cell lines when compared to lines of non-T lymphoid cell origin. In addition, DEAE-cellulose chromatography revealed a qualitative contrast of isoenzymic composition of protein kinase from these cell lines. Cyclic AMP-independent casein kinase activity was high in both types of cell lines. These results suggest that high protein kinase activity is characteristic of T cells and may be related to their higher sensitivity to cAMP agonists in comparison to non-T cells. This study also provides further evidence for an association between increased cAMP-independent protein kinase activity and the transformed state, which has been noted for a variety of other cell types. (Author abstract) (30 Refs)

## 28. ASSOCIATION OF IMPAIRED IMMUNE RESPONSIVENESS OF LYMPHOCYTES FROM ANIMALS BEARING LARGE TUMORS WITH A MEMBRANE-BOUND SUPPRESSIVE SUBSTANCE.

**Wang BS, Heacock EH, Onikul SR, Chang-xue Z, Young TH, Mannick JA**

**Chemotherapy Res. Dept., Lederle Lab., The American Cyanamid Co., Pearl River, NY, 10965**

**Cancer Res; 42(2):416-420 1982**

The immunoreactivity of lymphocytes from mice bearing large tumors was investigated. As compared to normal lymphocytes, lymphocytes from tumor bearers manifested a lessened proliferative response to T-cell mitogens and were less capable of destroying syngeneic tumor target cells. However, the impaired reactivity of these lymphocytes was improved significantly after washing repeatedly in tissue culture medium in vitro. The increase in cytolytic activity was tumor specific. A membrane-associated suppressive substance was detected in the washing medium which inhibited the cytotoxicity of washed lymphocytes. The effect of suppressive substance was tumor specific and sensitive to treatment with protein A and anti-immunoglobulin antibody, indicating that the suppressive substance contained immunoglobulin. The present findings suggest that a membrane-associated suppressive substance(s) may be in part responsible for the diminished immune responsiveness of lymphocytes from animals bearing large tumors. (Author abstract) (23 Refs)

### 29. THE CHARACTERISTICS OF CELLS CULTURED FROM HUMAN NEUROBLASTOMA TRANSPLANTED INTO NUDE MICE AND THEIR SENSITIVITY TO ANTICANCER AGENTS (MEETING ABSTRACT).

Kukita K, Une Y, Sasaki F, Sato K, Hata Y, Uchino J
First Dept. Surgery, Hokkaido Univ., Sch. Medicine, Sapporo-shi, Hokkaido, 060, Japan
Shoni Gan; (16):13-14 1981

A Stage III (rosette forming type) neuroblastoma of a 4-yr-old girl who was repeatedly operated on was transplanted into nude mice from a lymph node metastasis. A piece of tissue was removed from the tumor after 10 generations, minced finely, and cultured in RPMI 1640 with 10% fetal calf serum after collagenase treatment. The growth curve was constant even at the 26th generation. Phase cont rast microscopy showed clear branch-like protuberances in the cells at the 10th generation, and the growth curve of the cells at the 23rd generation was logistic. The cytotoxicity of vincristine (VCR), active cyclophosphamide (CPM) and adriamycin (ADR) at 1 x 10(-4) -10(-1) ug/ml was determined, by using 3 x 10(4) cells of the 25th serially cultured generation, from the viability of the cells after 24-hr contact with the drugs. VCR had no clear cytotoxicity at a concentration of less than 10(0) ug/ml, but its cytotoxicity was clear at 10(1) ug/ml. CPM showed a clear cytotoxic effect at a concentration of 10(1) ug/ml or more. ADM had a dose-dependent cytotoxic effect at doses exceeding 10(-1) ug/ml. At hr 24 after treatment with VCR at various concentrations, the cells were fixed in 50% ethanol and stained with propridium iodide. The DNA histograms obtained by flow microfluorometry using a Biophysics 4800 showed that 10(-4) -10(-1) ug of VCR per ml caused accumulation of the cells at the G2M phase, suggesting the possibility of synchronization therapy. (no Refs) (In JPN)

### 30. SECRETION-ASSOCIATED LECTIN-BINDING SITES AS A PARAMETER OF HORMONE DEPENDENCE IN MAMMARY CARCINOMA.

Klein PJ, Vierbuchen M, Wurz H, Schulz KD, Newman RA
(c/o Newman) Membrane Immunology Lab., Imperial Cancer Res. Fund, Lincoln Inn Fields, London WC2A 3PX, England
Br J Cancer; 44(5):746-748 1981

Hormone dependency in mammary carcinoma was studied with the aid of lectins from peanut (PNA: peanut agglutinin) and Helix pomatia (HP), which have high affinities for D-galactosyl-(1-3)-N-acetyl-D-galactosamine and N-acetyl-D-galactosamine, respectively. Experiments were performed on formaldehyde-fixed tissue sections from 75 patients. After treatment of tissue sections with neuraminidase to expose any sialic acid-covered receptors, PNA binding was seen within cytoplasmic vacuoles of breast tissue with secretory malfunction; in well-differentiated carcinomas, binding to apical surfaces and on secretions lying within the glandular structures was observed. Of 46 specimens of mammary tumors, 68% had PNA receptors as well as estrogen (E) and progesterone (P) receptors. Only 45% had PNA receptors when only E receptors were detected. Only 23% of specimens with no detectable E or P receptors had PNA receptors. Greater PNA binding occurred in the primary tumors than in axillary-lymph node metastases. Responsiveness of 29 breast cancer patients to endocrine therapy was determined. Of lectin- (PNA and HP) positive patients, 82% showed a response to hormone therapy. Only 24% of the lectin-negative group showed similar responses. A poor correlation was found between lectin-receptor expression and response to chemotherapy. Results indicated that the lectin-binding method is a useful hormone-receptor assay. (7 Refs)

### 31. ANTIBODY-DEPENDENT CYTOLYSIS OF THE HUMAN LEUKEMIA CELL LINE K-562 IN THE ABSENC E OF EFFECTOR CELLS OR COMPLEMENT.

Wust CJ, Green M, Lozzio CB, Lozzio BB
Dept. Microbiology, Univ. Tennessee, Knoxville, TN, 37916
Blood; 59(1):133-140 1982

K-562 human leukemia cells grown in the presence of specific goat anti-K-562 gamma globulin, F(ab)'2' Fab', or Fab showed a decrease in DNA and protein syntheses and a loss of cell viability within several hr. Eventually all cells died and lysed within 2-5 days. These events occurred in the absence of added effector cells or complement. The effect on the cell was not due to proteolytic or other external lytic activity generated at the cell surface, since 51Cr-labeled bystander cells or antibody-sensitizer bystander cells (chicken erythrocytes or K-562 cells) were not lysed when added to cultures of K-562 cells incubated with immune globulin. The anti-K-562 gamma globulin was not observed to patch or cap on K-562 cells, but the ability of bound immunoglobulin to fix complement decreased markedly (50% in 60 min), so that no complement-mediated cytolysis could be observed at 2 hr. However, the immunoglobulin, at least portions of it, reacted with fluorescein-labeled rabbit anti-goat gamma globulin for about 16 hr. 125I-labeled immune globulin appeared to be internalized and released into the medium as small degradation products. 125I-labeled Fab did not appear to be internalized, since it was released intact and more rapidly from cells than the intact globulin. (Author abstract) (23 Refs)

## LYMPHOCYTE AND DIFFERENTIATION ANTIGENS

### 32. FURTHER BIOCHEMICAL CHARACTERIZATION OF THE HUMAN THYMOCYTE DIFFERENTIATION ANTIGEN T6.

van Agthoven A, Terhorst C
(c/o Terhorst) Div. Tumor Immunology, Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115
J Immunol; 128(1):426-432 1982

Charge heterogeneity of the human thymocyte antigen T6 was studied by isoelectric focusing and two-dimensional gel electrophoresis. The larger subunit of T6 (a 49,000 mol wt glycoprotein) contained several oligosaccharide side chains bearing up to 12 terminal sialic acids. When T6 antigens from 19 individual thymuses were analyzed, no differences in the isoelectric focusing patterns of the larger subunit could be detected. The larger subunit of the T6 antigen from MOLT-4 cells (52,000 mol wt) contained an extra oligosaccharide if compared with the T6 antigen from thymus or three other T leukemic cell lines. Two types of small subunits of T6 were found. In addition to a protein of mol wt 12,000, pl 5.5 identified as beta2-microglobulin, a (mol wt 12,000, pl 7.0) nonglycosylated protein, was detected on two dimensional gels. This protein does not cross-react with beta2-microglobulin, and its amount varied in different T6 preparations. The tissue distribution, the mol wt the association with beta2-microglobulin and the limited structural heterogeneity of T6 support the idea that T6 is the human homologue o f the murine thymus leukemia antigen (TL). (Author abstract) (36 Refs)

## 33. SEROLOGICAL AND FUNCTIONAL CHARACTERIZATION OF HUMAN T CELL SUBSETS.

Pandolfi F, Strong DM, Slease RB, Bonnard GD
Div. Infectious Diseases II, Inst. Internal Medicine III, Univ. Rome, 00161 Rome, Italy
Clin Exp Immunol; 43(2):319-328 1981

Two specific rabbit sera against human T cells, one raised against fetal thymocytes (anti-HTY) and one raised against human cultured T cells (anti-CTC), were studied. Antisera were produced by injecting New Zealand white rabbits with fetal thymocytes or with T cells cultured in the presence of conditioned medium from peripheral blood mononuclear lymphocytes (PBL) stimulated by phytohemagglutinin. After a series of absorptions by a variety of neoplastic hemopoietic cell lines, anti-HTY and anti-CTC each showed cytotoxicity against T cells but not against B cells or null cells. In fluorescence-activated cell-sorter analyses, T cells showed a higher fluorescence intensity with the antisera than did B cells. After absorption with T chronic lymphocytic leukemia (T-CLL) cells, anti-HTY was active against thymocytes, with 40-50% of normal T-PBL, and with T cells whose rosette-forming capacity with sheep RBC was not inhibited by theophylline. PBL remaining after preincubation with anti-HTY and complement showed reduced sensitivity to stimulation by lectin or mixed lymphocyte culture (MLC), but were responsive to tetanus toxoid (t tox) After absorption with MOLT-4 cells, anti-CTC was active against 30% of T-PBL and most T-CLL cells with Fc receptors. PBL remaining after preincubation with this adsorbed serum showed enhanced sensitivity to stimulation by lectin, t tox, and MLC. Results demonstrate the existence of two distinct major subpopulations of human T cells. (33 Refs)

## 34. HYBRIDOMA MONOCLONAL ANTIBODIES IN THE ANALYSIS OF HUMAN CELL SURFACE ANTIGENS.

Levy R, Bergman Y, Finn O
Dept. Medicine, Div. Oncology, Stanford Univ. Medical Center, Stanford, CA, 94305
In Vitro; 17(12):1051-1057 1981

In the present paper, we will summarize studies we have performed on two distinct human lymphocyte cell surface antigens defined by monoclonal antibodies: Leu-1 and HLA-DR. (Author abstract) (27 Refs)

## 35. THE REACTION SPECIFICITY OF VARIOUS MONOCLONAL ANTIBODIES AND CELLULAR ORIGIN AND DIFFERENTIATION OF CULTURED CELL LINES DERIVED FROM HUMAN LEUKEMIAS AND LYMPHOMAS.

Tobinai K, Hirose M, Minato K, Shimoyama M
(c/o Shimoyama) Section Hematology, Natl. Cancer Center Hosp., 1-1, Tsukiji 5-chome, Chuo-ku, Tokyo 104, Japan
Jpn J Clin Oncol; 11(3):469-479 1981

Human hemopoietic tumor-cell lines (6 T-cell; 10 B-cell; 5 non-T, non-B-cell; 2 myeloid; 2 monocytoid) were grown exponentially, and their reactions to 12 monoclonal antibodies (OKT 3, OKT 4, OKT 6, OKT 8, OKI 1, OKM 1, anti-Leu-1, 10.2, (antihuman Lyt 2), 9.6 (antihuman Lyt-3), anti-B1, J5, anti-Mo 1) were evaluated by indirect immunofluorescence assay and by rosette-forming capacity with sheep erythrocytes, human T-lymphocyte antigen, Ia-like antigen, and surface immunoglobulins. The reactivities of the monoclonal antibodies were highly specific against cultured leukemia and lymphoma cell lines, with a few exceptions, which are described. The titer of the antibody differed among the cell lines, indicating that while use of the monoclonal antibodies specific for certain differentiation antigens may be useful for elucidating the cellular origin, stage of differentiation, and subset identification of human hemopoietic tumor cells, the titration of each monoclonal antibody requires the use of several cultured cell lines in order to determine an appropriate concentration for clinical use. (42 Refs)

## 36. THE VALUE OF A NEW B-CELL SPECIFIC MONOCLONAL ANTIBODY IN COMBINATION WITH CONVENTIONAL IMMUNOLOGIC MARKERS FOR TYPING OF MALIGNANT NHL (MEETING ABSTRACT).

Obrecht JP, Christen D, Forster HK, Gudat FG
Division Oncology and Institute for Pathology, University of Basle, Basle, Switzerland
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Results obtained by a new B-specific monoclonal antibody were compared to those of conventional marker analysis (rosette formation with sheep and mouse RBC, sIg, Fc-receptor) in 32 patients (pat) with malignant Non-Hodgkin's lymphoma (NHL). This monoclonal antibody, anti-Y29/55, was produced by fusion between a mouse myeloma cell line and splenocytes of a mouse immunized to peripheral blood lymphocytes (PBL) of a patient with untreated chronic lymphocytic leukemia (CLL). Previous experiments had shown that this antibody reacted with normal sessile B-lymphocytes but not with non-neoplastic B-cells circulating in blood. The following results were obtained by conventional marker typing: 15 CLL were of the B-cell type. Eleven NHL (5 lymphocytic poorly differentiated, 2 lymphohistocytic, 3 histiocytic and 1 Burkitt's lymphoma) were positve for B-markers. Four NHL (2 lymphocytic poorly differentiated, 1 lymphohistiocytic, 1 histiocytic) were of the T-cell type. Two histiocytic NHL did not express B- or T-markers. The monoclonal antibody detected all B-cell lymphomas in blood and/or tissue. Additionally 1 of the histiocytic lymphomas which was negative to conventional markers reacted with anti-Y29/55. The antibody did not react with T-cell lymphomas. (no Refs)

## 37. SURFACE EXPRESSION OF ALIEN HYBRID IE/C ANTIGENS ON THE RETICULUM CELL SARCOMA OF SJL/J MICE.

Bonavida B, Wilbur SM, Marelli O, Martin WJ, Uhr JW
Dept. Microbiology and Immunology, UCLA Sch. Medicine, Los Angeles, CA, 90024
Transplant Proc; 13(4):1833-1836 1981

The biologic and molecular nature of the murine response elicited by spontaneous tumors in SJL/J mice was investigated. Reticulum cell sarcoma (RCS) tumors expressed IE/C antigens that are alien to the host SJL/J; the antigens are not normal membrane constituents of host SJL/J cells. Investigations demonstrated the expression of alien H-2d specificities on RCS cells by serologic, cell-mediated, and immunological assay The detection of alien H-2 specificities on RCS tumor cells varied with different assays according to the origin of RCS tumor cells. SJL/J anti-DBA/2 lymphocytes (from 4-day mixed lymphocyte reaction) bound H-2d and RCS tumor cells but not SJL/J or cells from other haplotypes. The syngeneic antitumor lymphocytes apparently have receptors for tumor associated antigen cross-reactive with H-2d specificities. Antigens recognized by the antitumor lymphocyte were analyzed using recombinant strains of mice. RCS antigens expressed hybrid Ia antigens encoded by the IE/C subregion of the major histo-

compatibility complex. The Ia.7 specificity was expressed on the component of hybrid Ia molecules regardless of haplotype. Experiments suggest that the RCS tumors absorbed the Ia.7 specificity. SJL/J and C57BL/6 (lacking Ia.7 specificity) did not absorb the cytotoxic activity. Results suggest that RCS tumors express on their surface IE/C antigens serologically identical to IE/C antigens of other H-2 haplotypes. (13 Refs)

### 38. ADHERENT IA+ MURINE TUMOR LINES WITH CHARACTERISTICS OF DENDRITIC CELLS. I. MORPHOLOGY, SURFACE PHENOTYPE, AND INDUCTION OF SYNGENEIC MIXED LYMPHOCYTE REACTIONS.

**Cohen DA, Kaplan AM**
**Dept. Surgery, MCV/VCU Cancer Center, Medical Coll. Virginia, Virginia Commonwealth Univ., Richmond, VA, 23298**
**J Exp Med; 154(6):1881-1898 1981**

Several adherent cell lines cloned from mouse P388 leukemia were isolated and characterized. The cell lines were morphologically and functionally similar to dendritic cells (DC) of the spleen with respect to dendritic processes, large numbers of mitochondria, surface expression of immune region-associated (Ia) antigens, and induction of syngeneic and allogeneic mixed lymphocyte reactions. Of adherent P388 cells, 24-69% were positive for Ia antigen, greater than 95% were positive for major histocompatibility D, splenic macrophage-associated, and T cell-associated antigens, and 0% were positive for surface immunoglobulins; positive values were obtained in 13-42%, greater than 95 %, 0, greater than 95%, and 0%, respectively, of nonadherent cells. Both adherent and nonadherent forms of P388 expressed Ia antigens, with a broad range of fluorescent intensity within each respective clone. Cell-to-cell variability of surface Ia antigens in both adherent and nonadherent cells was also detectable with antisera against I-A sub region antigens. Adherent cells strongly stimulated syngeneic and allogeneic T lymphocyte proliferation in the absence of antigen; cytotoxic T cells directed against the stimulators were induced only during allogeneic stimulation. Nonadherent P388 clones did not stimulate either allogeneic or syngeneic T cell proliferation. (28 Refs)

### 39. RECOGNITION OF POLYMORHPIC H2 DOMAINS BY T LYMPHOCYTES. I. FUNCTIONAL ROLE OF DIFFERENT H-2 DOMAINS FOR THE GENERATION OF ALLOREACTIVE CYTOTOXIC T LYMPHOCYTES AND DETERMINATION OF PRECURSOR FREQUENCIES.

**Weyand C, Goronzy J, Hammerling GJ**
**Institut fur Immunologie und Genetik, Deutsches Krebsforschungszentrum, Heidelberg, W. Germany**
**J Exp Med; 154(6):1717-1731 1981**

The fine specificity and receptor repertoire of cytotoxic T lymphocytes (CTL) was examined. Murine histocompatibility complex (H-2) Kk CTL clones were generated in a limiting dilution system and their fine specificity assessed by target inhibition with a panel of monoclonal (mc) anti-H-2Kk antibodies. Poisson distribution analysis yielded three straight lines, indicating the existence of three precursor populations differing in precursor frequency. Av frequency data were 1/400 for CTL I, 1/2,000 for CTL II, and 1/4,000 for CTL III. Limiting dilution curves suggested that the more frequent CTL populations were subject to a suppressive mechanism. Biphasic curves represented CTL I and II in some experiments and CTL II and III in others. Results of target inhibition studies with a panel of mc anti-H-2Kk antibodies that had previously been shown to define two separate clusters of antigenic determinants on the Kk molecule indicated that CTL subsets differ in their receptor repertoire. Application of a single antibody blocked only a fraction of CTL clones, whereas CTL target interaction was totally prevented when numerous epitopes were covered by a mixture of mc antibody or by an alloantiserum. Each antibody exhibited a characteristic inhibition pattern. Thus, each CTL subpopulation appears to consist of various different clonotypes with specificity for different target epitopes. Generation of CTL subpopulations with specificity for particular domains may be controlled by suppressive mechanisms. The data suggest that CTL recognize basically the same polymorphic domains on the H-2Kk molecule defined by antibodies; regulatory mechanisms apparently determine the expressed repertoire in CTL populations. (25 Refs)

### 40. QUANTITATIVE VARIATIONS IN THE EXPRESSION OF H-2 ANTIGENS ON MURINE LEUKEMIA VIRUS-INDUCED TUMOR CELLS CAN AFFECT THE H-2-RESTRICTION PATTERNS OF TUMOR-SPECIFIC CYTOLYTIC T LYMPHOCYTES.

**Plata F, Tilkin AF, Levy JP, Lilly F**
**Unite d'Immuno-Parasitologie, Institut Pasteur, 25 rue du Docteur Roux, 75015 Paris, France**
**J Exp Med; 154(6):1795-1810 1981**

Expression of major histocompatibility antigens (H-2) Kd and Dd was quantified i n three different leukemia cell lines induced by Gross murine leukemia virus (MuLV) in BALB/c (H-2d) mice. Preferential recognition of Gross MuLV-induced tumor antigen with H-2Kk or H-2Dd antigen by tumor-specific cytotoxic T lymphocytes (CTL) from BALB/c mice was correlated with the quantitations. The three BALB/c tumor lines differed in amount of H-2Kd and H-2Dd antigens expressed on the cell surface; the variations were reflected in quality as target cells to Gross MuLV-specific CTL from BALB/c mice. The results indicated that restriction of tumor-specific CTL activity by H-2 can be directed at the target cell level by the quantitative modulation of H-2K or H-2D antigen expression; separate tumors induced by the same MuLV in the same or in H-2-congeneic strains of mice may vary in absolute amount of H-2K or H-2D antigen expressed on the cell surface. (35 Refs)

### 41. TUMOR IMMUNITY TO MURINE PLASMA CELL TUMORS. VII. EXPRESSION OF H-2 AND TUMOR ANTIGENS ON IG SYNTHESIS VARIANTS OF MPC-11.

**Giorgi JV, Burton RC, Scott D, Warner NL**
**Transplantation Unit, Dept. Surgery, Massachusetts General Hosp., Boston, MA**
**Int J Cancer; 29(1):119-126 1982**

As a part of our continuing investigations directed toward defining the nature of the antigens on murine plasmacytomas (PCT), MPC-11 and two immunoglobulin (Ig) synthesis variants of this cell line were examined for H-2 and tumor-associated antigen (TAA) expression, and for the possible role of H-2 in the cytotoxic T lymphocyte response to TAA. The tumor lines studied were MPC-11 (an IgG2b producer), MPC-11.662 (a variant which produces only light chains), and NP.2 (a variant which produces neither Ig chain). Both H-2 expression, which was analyzed by flow cytometry and by cold target cell blocking of the activity of cytotoxic T lymphocytes (CTL) generated in allogeneic cultures, and TAA expression, which was analyzed by cold target cell blocking of the activity of tumor-specific CTL generated in syngeneic cultures, were found to be quantitatively similar on the three lines. When a possible association between H-2 and TAA expression was ex-

amined by testing the ability of anti-H-2 sera to block tumor-specific CTL directed against MPC-11, no association between H-2 and TAA was detected. The results of these studies provide new information about H-2 and TAA expression on murine PCT. Furthermore, they suggest that changes in H-2 and TAA expression which have been reported to sometimes accompany loss of Ig synthesis may represent independent genetic, phenotypic, or metabolic variations, rather than alterations linked to the loss of Ig synthesis. In addition, these results, in agreement with our previous studies on MPC-11, support the concept that there is not an obligatory association of TAA with H-2 on the surface of murine PCT. Because these results differ from those reported in some other systems in which an association between H-2 and TAA on murine PCT was demonstrated, it must be emphasized that the TAA of PCT appear to be quite heterogeneous, and more investigations will be necessary in order to clearly define these antigens and the T-cell response to each of them. (Author abstract) (41 Refs)

### 42. CHARACTERIZATION OF ALLOANTIGEN-ACTIVATED HUMAN LYMPHOCYTES CYTOTOXIC FOR AUTOLOGOUS EB VIRUS-TRANSFORMED LYMPHOBLASTOID CELL LINES.

**Zarling JM, Ferrone S, Bach FH, Gillis S, Meruelo D, Martin WJ**
**Immunology Res. Center, Dept. Lab. Medicine/Pathology, Univ. Minnesota, Minneapolis, MN, 55455**
**Transplant Proc; 13(4):1893-1896 1981**

Previously reported results on the ability of cytotoxic T lymphocytes (Tc) or natural killer (NK)-like cells to mediate lysis of autologous Epstein-Barr virus-transformed lymphoblastoid cell lines (LCL) by lymphocytes stimulated with pooled allogeneic normal cells are summarized. Studies of the effect of 5-bromodeoxyuridine and light on generation of cytotoxic cells capable of lysing autologous LCL cells indicated that alloantigen-induced effector cells that lyse autologous LCL cells are similar to those lysing allogeneic normal cells. Treatment of fresh lymphocytes with monoclonal antibody OKT3 (reactive with greater than 95% of RBC-rosetting cells) or OKT8 (reactive with a subpopulation of T cells) and complement (C') did not reduce NK activity against K562 leukemia cells. Treatment of fresh lymphocytes with monoclonal antibody OKM1 (reactive with macrophages and a small proportion of nonadherent cells) and C' decreased NK cell activity by approx 75%. Thus the majority of NK cells appear to be OKT3-, OKT8-, OKM1+. The phenotype of mixed WBC culture (MLC)-generated cells that lyse autologous LCL was the same as that of Tc which lyse allogeneic normal cells (OKT3+, OKT8+); NK-like cells generated in MLC, which lyse K562 cells, were OKT3-, OKT8-. The results indicate that lysis of autologous LCL cells by pool-stimulated cells is mediated by Tc. (16 Refs)

### 43. SURFACE PROTEIN ABNORMALITIES IN LYMPHOCYTES AND PLATELETS FROM PATIENTS WITH WISKOTT-ALDRICH SYNDROME.

**Parkman R, Remold-O'Donnell E, Kenney DM, Perrine S, Rosen FS**
**Div. Immunology, Children's Hosp. Medical Center, Boston, MA, 02115**
**Lancet; 2(8260):1387-1389 1981**

Lymphocytes from three patients with the Wiskott-Aldrich syndrome were subjected to surface radioiodination and their 125I-labeled surface proteins were analyzed by SDS-polyacrylamide gel electrophoresis and autoradiography. Autoradiographs demonstrated the absence in all three patients of an 125I-labeled protein, mol wt 115,000, that was present in normal individuals. In addition, one patient had an additional labeled protein, mol wt 135,000, not found in normal individuals. The platelets from one patient were radioiodinated and the 125I-labeled membrane proteins were analyzed. Glycoproteins Ia and Ib were reduced in amount and restricted in heterogeneity while glycoproteins IIb and IIIa were normal. These results suggest that the primary defect in the Wiskott-Aldrich syndrome may be abnormalities of (glyco)proteins normally present on the surface of lymphocytes and platelets. (Author abstract) (15 Refs)

### 44. STIMULATION BY CLL CELLS IN MIXED LYMPHOCYTE CULTURE (MLC).

**Jones EH, Hockley AB, Lawler SD**
**Dept. Cytogenetics and Immunogenetics, Inst. Cancer Res., Royal Marsden Hosp., London SW3 6JJ, England**
**Br J Cancer; 44(5):675-681 1981**

Cells from patients with chronic lymphocytic leukemia (CLL) do not respond in the mixed lymphocyte culture (MLC) but are able to stimulate the response of normal lymphocytes. Mixed lymphocyte cultures were performed using cells from 24 patients with CLL and cells from 16 normal donors. The stimulatory capacity of eight of these CLL cells was reduced when a common DR antigen was shared with the normal responding cell. We suggest that cells from certain selected CLL patients may be used in the mixed-lymphocyte reaction for determining the D-locus specificity of normal donors. CLL cells which expressed one DR antigen only, induced more clearly defined typing responses than cells with two DR antigens. There was no correlation between the ability of a CLL cell to induce a typing response and the T-cell status of the patient. However, a correlation with clinical course was suggested, because most cells which induced a typing response were obtained from patients who had received intensive treatment for the disease. (Author abstract) (21 Refs)

## CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION

### 45. MODULATION OF T LEUKAEMIC CELL PHENOTYPE WITH PHORBOL ESTER.

**Della D, Greaves MF, Newman RA, Sutherland DR, Minowada J, Kung P, Goldstein G**
**Membrane Immunology Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London, England**
**Int J Cancer; 29(1):23-31 1982**

A panel of monoclonal antibodies and other markers (eg, terminal deoxynucleotidyl transferase, sheep erythrocyte rosettes, peanut agglutinin) have been used in conjunction with flow cytometry and biochemical analysis to monitor the induction of maturation in human thymic (T) leukemic cell lines by phorbol ester (TPA). Seven cell lines underwent multiple phenotypic alterations in response to TPA but were unresponsive to synthetic thymic hormones (TP5, FTS) or to other compounds (eg, DMSO, retinoic acid) which induce maturation in other types of leukemia. The changes parallel those observed in normal T-cell differentiation and partly reflect alterations in glycosyl transferase activity, altered synthesis of proteins and regulation of cell surface receptors (for transferrin) associated with rapid growth and metabolism. These studies further illus-

trate the reversibility of maturation arrest in human leukemia and provide support for the view that leukemia may involve regulatory defects in the coupling of proliferation and maturation. Induction or promotion of terminal differentiation in leukemic equivalents of T-cell precursors may provide a convenient system for the study of biochemical and molecular events involved in T-cell development and diversification. (Author abstract) (72 Refs)

## 46. STUDIES OF HUMAN LEUKEMIC LYMPHOID PROGENITOR CELL DIFFERENTIATION WITH THE PHORBOL ESTER TPA (MEETING ABSTRACT).

**LeBien TW, Boue DR, Kersey JH**
**Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, MN**
**Tenth Annual Meeting, Midwest Autumn Immunology Conference, Oct 18-20, 1981, Minneapolis, Minnesota University of Minnesota; 1981**

A major problem plaguing studies of human lymphoid progenitor cells has been the small number of these cells present in normal bone marrow (BM) and the paucity of assays for analyzing their various differentiation pathways. Since the cells involved in non-T, non-B (E-, SIg-) acute lymphoblastic leukemia (ALL) have been hypothesized to represent the malignant counterparts of BM lymphoid progenitor cells, ALL cells may be helpful in studying human lymphopoiesis. We have approached this problem using a panel of cell markers and the phorbol ester 12-O-tetradecanoylphorbol-13-acetate (TPA). Results to be presented clearly show that TPA can induce a number of phenotypic changes in non-T, non-B ALL cells. Such changes may reflect a differentiation-linked expression of cellular structures in normal BM lymphoid progenitor cells. (no Refs)

## 47. LYMPHOCYTE DIFFERENTIATION AND MALIGNANT LYMPHOMA.

**Kikuchi K, Ishii Y, Koshiba H**
**Dept. Pathology, Sapporo Medical Coll., Sapporo, Japan**
**Nippon Ketsueki Gakkai Zasshi; 44(7):1384-1394 1981**

Diagnostic and immunopathologic application of xenoantisera against human normal and neoplastic T and B cells, immunochemical characterization of lymphocyte surface antigens, establishment of B cell hybridomas secreting monoclonal antibodies to lymphocyte differentiation antigens, and analogy of mouse to human lymphocyte differentiation antigens and their distribution in normal and neoplastic immune systems are discussed. Lymphocyte differentiation and malignant lymphomas were studied using 50 hematopoietic cell lines. Cell lines were used to determined to what kind of differentiation stage the antigen belonged, the differentiation stages having been defined with xenoantisera or monoclonal antibodies. Stages of lymphocyte ontogeny were determined with the use of lymphocyte markers, differentiation antigens defined by monoclonal antibodies and conventional antisera. Results showed that lymphoid malignancies reflect the same degree of heterogeneities in maturation as seen in normal lymphocyte differentiation, and each of them can belong to a specified compartment. Relationship among possible compartments of T and B cell differentiation, leukemia-lymphomas and cell surface markers is presented. Malignant lymphomas and leukemias are easily diagnosed and classified according to their cell surface phenotype, and may be considered as clonal expansions of the specific normal anatomic and functional components of the immune system under 'frozen' differentiation. Surface phenotypes might reflect the clinical and pathologic expressions in patients with malignant lymphomas and leukemias with these phenotypes. (15 Refs)

## 48. SURFACE GLYCOPROTEINS OF NORMAL AND MALIGNANT HEMATOPOIETIC CELLS.

**Andersson LC**
**Pathology Inst., Helsinki Univ., 00290 Helsinki 29, Finland**
**Duodecim; 97(18):1509-1518 1981**

Surface glycoprotein (GP) analysis was used to classify normal and malignant hematopoietic cells and to measure their degree of differentiation; the technique may be of importance in the prognosis and treatment of various types of leukemia. When GP120 becomes GP130 in the conversion of T-lymphocytes to killer cells, a definite change occurs in glycosylation, altering electrophoretic mobility. GP130 is specifically bound to the lectin of Vicia villosa, but the lectin does not react with GP120. When the promyelocyte grows into a granulocyte, the disappearance of GP160 and the appearance of GP130 is an example of altered glycosylation. Since GP160 and GP130 both react to the same antiserum, they clearly possess a common peptide component. Changes linked to differentiation during the glycosylation of surface glycoproteins can lead to the formation of differentiation antigens, important indicators of interaction between cells. A considerable part of the genetic information that measures surface changes in the cell during growth could be transmitted by way of various carbohydrate transferases. (22 Refs) (In FIN)

## 49. ELECTROPHORETIC MOBILITY PROFILES OF MOUSE LEUKEMIAS: I. ELECTROPHORESIS OF NORMAL MOUSE THYMUS AND LYMPH NODE CELL POPULATIONS.

**Bubenik J, Bubenikova D, Lastovicka J, Jandlova T**
**Inst. Molecular Genetics, Czechoslovak Acad. Sciences, 160 00 Prague 6, Czechoslovakia**
**Neoplasma; 28(5):517-525 1981**

Anodic electrophoretic mobility of thymocytes and lymph node cells from random-bred ICR Swiss mice was examined. Three cell populations were identified which differed in their surface charge as reflected in their distinct mean AEM and in their time of appearance during the course of life. The first electrophoretically slow-moving population with a mean AEM of 0.97 um sec-1 V-1 cm was detected in the early postnatal period. In the 1st mo after birth, the first population was replaced by a second, slower-moving population with a mean AEM of 0.83 um sec-1 V-1 cm. In the second mo after birth, a third, fast-moving population with a mean AEM value of 1.24 um sec-1 V-1 cm appeared in addition to the second cell population. The third population constituted only a minority of thymus cells and continued to be present, as well as the second cell population, up to 2 yr of age. Lymph node cells of ICR mice showed a typical bimodal electrophoretic distribution; fast LNC displayed a mean AEM of 1.18 um sec-1 V-1 cm whereas slow LNC displayed a mean AEM of 0.76 um sec-1 V-1 cm. The percentage of cells in the fast- and slow-moving LNC subpopulations was similar to the expected percentage of T and B LNC. Fractionation of the ICR LNC on nylon wool columns revealed that the majority of the fast-moving LNC corresponded to the nonadherent Thy 1.2+ lymphocytes and the majority of the slow-moving LNC to the nylon wool-adherent sIg+ lymphocytes. (Author abstract) (31 Refs)

## 50. NK CELL SENSITIVITY OF THE LEUKEMIC K 562 CELLS; EFFECT OF SODIUM BUTYRATE AND HEMIN INDUCTION.

**Dokhelar MC, Testa U, Vainchenker W, Finale Y, Tetaud C, Salem P, Turaz T**
**(c/o Turaz), Institut Gustave-Roussy, Rue Camille Desmoulins, 94800 Villejuif, France**
**J Immunol; 128(1):211-216 1982**

Two differentiation inducers, hemin and sodium butyrate, have been studied for their effect on the NK sensitivity of human leukemic K 562 cells. When cultivated in the presence of 0.1 mM hemin, K 562 cells increased their hemoglobin synthesis. However, their susceptibility to NK lysis remained unaffected. On the other hand, sodium butyrate, which is known as a more potent differentiating agent, consistently reduced the NK sensitivity of K 562 cells and simultaneously induced the appearance of several differentiation markers. The effect of sodium butyrate on NK sensitivity was dose-dependent (maximal action at a 2-mM concentration), appeared after 2 days in culture, and was maximal after 5 days. After sodium butyrate removal from the culture medium, K 562 cells recovered their normal NK susceptibility within 4 days. In cold-target competition experiments, untreated K 562 cells acted as better competitors than butyrate-treated K 562 cells. Target-binding cell assays and specific NK cell removal on K 562 monolayers demonstrated that NK cells were less adherent to butyrate-treated than to control K 562 cells. From these data, it could be postulated that sodium butyrate modulates the expression of some target structure(s) involved in NK target binding. Five subclones of K 562 have been selected for exhibiting distinct, stable properties with regard to their cellular commitment (either to erythroid or to megakaryocytic lineage). The NK sensitivity of these subclones was roughly identical, and in all of them, butyrate treatment induced similar protection against NK-mediated lysis. Thus, the susceptibility to NK lysis and its modulation did not depend up on the predominant lineage present in each clone. (Author abstract) (32 Refs)

## 51. STIMULATED MACROPHAGES EXPRESS A NEW GLYCOPROTEIN RECEPTOR REACTIVE WITH GRIFFONIA SIMPLICIFOLIA I-B4 ISOLECTIN.

**Maddox DE, Shibata S, Goldstein IJ**
**(c/o Goldstein) Dept. Biological Chemistry, Univ. Michigan, Ann Arbor, MI, 48109**
**Proc Natl Acad Sci USA; 79(1):166-170 1982**

This paper presents data on reactions of murine macrophages with a variety of lectins, with special focus on Griffonia simplicifolia I-B4 isolectin, the only lectin we tried that distinguishes stimulated macrophages from resident populations. Specificity of Griffonia simplicifolia I reaction with carbohydrate determinants at the cell surface is shown by (i) ability of alpha-galactosidase treatment of intact cells to abolish all lectin binding whereas beta-galactosidase has no effect on lectin binding, (ii) ability of methyl alpha-D-galactopyranoside to completely inhibit lectin binding with methyl alpha-D-glucopyranoside having no effect on lectin binding, (iii) ability of brief treatment of intact cells with trypsin to liberate a glycopeptide that reacts with G simplicifolia I to form a precipitate that is dissolved by addition of methyl alpha-D-galactopyranoside or alpha-galactosidase but not by addition of methyl alpha-D-glucopyranoside or beta-galactosidase, (iv) ability of methyl alpha-D-galactopyranoside (but no other monosaccharide) to completely inhibit avid binding of macrophages to G simplicifolia I lectin immobilized on an insoluble support, and (v) ability of immobilized lectin to separate macrophages into highly pure subpopulations of lectin-reactive and lectin-unreactive cells, as shown by examination of fluorescein-labeled lectin-treated cells with phase-contrast/fluorescence microscopy. (Author abstract) (16 Refs)

## 52. ACTIVATION OF HUMAN LYMPHOCYTES BY CONCANAVALIN A OR PURIFIED PROTEIN DERIVATIVE RESULTS IN NO ALTERATION OF FLUORESCENCE POLARIZATION OF LIPID PROBES ALTHOUGH THE ELECTROPHORETIC MOBILITY OF THE CELLS IS CHANGED.

**Parola AH, Kaplan JH, Lockwood SH, Uzgiris EE**
**Dept. Chemistry, Ben-Gurion Univ. of Negev, Beer-sheva 84120, Israel**
**Biochim Biophys Acta; 649(3):616-624 1981**

Upon stimulation with either concanavalin A or the tuberculin antigen, purified protein derivative, human peripheral blood lymphocytes, purified on Ficoll-Hypaque, did not exhibit a concomitant lipid fluidity alteration as measured by fluorescence polarization (P) of the lipid probe, 1,6-diphenyl-1,3,5-hexatriene (DPH). This result was independent of the incubation period, ranging from 10 min to 72 hr. However, a general reduction in polarization value, from $p = 0.287$ (maintained for up to 2 hr of incubation) to $p = 0.225$ after 20 hr was observed for both experimental and control samples. Moreover, fluorescence polarization studies of the nonpenetrating modified DPH cationic lipid probe, 1-[4'-trimethylaminophenyl]-6-phenyl-1,3,5-hexatriene (TMA-DPH), also failed to show any change in lipid fluidity subsequent to a 1-3 hr incubation of lymphocytes with concanavalin A. Cell electrophoretic mobility, however, was altered (mean cell mobility increased by 10-15%) in a fast response to stimulation and was observed within several hours of in vitro application of concanavalin A and purified protein derivative. This initial response disappeared with further incubation at 37 C (greater than 3 hr) and was followed by a decline of cellular mobility of the concanavalin A-exposed cells after 48 and 72 hr of incubation. The unstimulated control cells did not change in mobility as a function of incubation time. The slow decline in mean cell mobility of the experimental cells is believed to be associated with blastogenesis. It is concluded that neither blastogenic transformation nor short term membrane alterations associated with human lymphocyte activation lead to lipid fluidity changes as measured in steady state by the fluorescence polarization of both DPH and TMA-DPH. (Author abstract) (41 Refs)

## 53. SPONTANEOUS CELL-MEDIATED CYTOTOXICITY IN PATIENTS WITH TRANSITIONAL CELL CARCINOMA OF THE URINARY BLADDER. DIFFERENCE IN EFFECTOR CELL POPULATION.

**Moroz C, Lindner A, Twig S, Madgar I, Many M**
**Rogoff-Wellcome Medical Res. Inst., Beilinson Medical Center, Petah-Tikva, Israel**
**Cancer Immunol Immunother; 12(1):57-62 1981**

Spontaneous lymphocyte-mediated cytotoxicity (SLMC) of peripheral blood lymphocytes (PBL) from patients (male, av age 71) with transitional cell carcinoma (TCC) of the urinary bladder was studied. SLMC of PBL against K-562 cells varied greatly, but PBL from controls and patients did not differ in cytoxic activity over a range of effector:target ratios. Following separation of effector cells into T and non-T fractions, SLMC of T lymphocytes derived from TCC patients was significantly greater than that of non-T cell populations. In controls, cytotoxic activity of non-T cells was higher than that of T cells. Repeated experiments on two TCC patients over a 1 yr period consistently showed the high SLMC of T lympho-

cytes. The relatively higher SLMC of T cells from TCC patients was even more profoundly exhibited when Peer cells instead of K-562 cells were targets. Neither treatment with monoclonal antibodies OKT 8 or OKT 4 and complement nor use of preparations depleted of Fc-receptor-positive cells could abolish the cytotoxicity of T cells from cancer patients. The natural killer-like T cells are thought to be a disease-related phenomenon, but their nature remains unclear. (35 Refs)

### 54. FUNCTIONAL CHANGES OF MACROPHAGES FROM POLYOMA TUMOR-BEARING MICE.

**Pituch-Noworolska A, Pajdak E**
**Div. Clinical Immunology and Microbiology, Inst. Pediatrics, Wielicka 265, 30-66 3 Krakow, Poland**
**Arch Immunol Ther Exp (Warsz); 29(4):423-429 1981**

CBA mice were inoculated with different doses of polyoma tumor cells. The PHA response of spleen cells from tumor-bearers was decreased but the spontaneous incorporation of 3H-leucine was increased. PHA-induced cytotoxicity of spleen cells was increased only in tumor-bearers. The expression of Fc receptors showed a slight increase on adherent cells from spleen and peripheral blood mononuclear cells under suboptimal conditions for EA rosette formation (small amount of antibody for coating the erythrocytes). The non-specific esterase activity was assayed in an extract of peritoneal macrophages and the elevated activity with isoenzymes was seen in a group of tumor-bearers. The results suggest a functional alteration of macrophages in polyoma tumor-bearing mice. (Author abstract) (24 Refs)

## EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS

### 55. EFFECT OF HYPERTHERMIA ON HOST IMMUNOCOMPETENCE: EXPERIMENTAL STUDIES ON THE EFFECT OF IN VITRO HEATING ON MURINE AND HUMAN LYMPHOCYTE FUNCTION.

**Izumi A, Osaki Y, Kanayama H, Shimizu N, Maeta M, Koga S**
**First Dept. Surgery, Tottori Univ. Sch. Medicine, Tottori, Japan**
**Gan No Rinsho; 27(15):1820-1824,A-89 1981**

Viability of mouse lymphocytes was reduced after in vitro heating (39 and 42 C, 1-5 hr) and was time and temperature-related. Hyperthermia (HP) depressed both cytotoxic activity of lymphocytes against MH-134 cells and phytohemagglutinin-induced blastogenesis. HP (42 C) also markedly decreased E-rosetting and blastogenesis of human lymphocytes. In some instances, human lymphocyte blastogenesis was enhanced after heating at 39 C. Results suggest hyperthermia may inhibit DNA synthesis in lymphocytes and cause damage to receptor sites. (14 Refs) (In JPN)

### 56. ALTERED SURFACE CHARACTERISTICS OF LYMPHOCYTES FROM PATIENTS HAVING ORAL CARCINOMA.

**Vijayakumar T**
**Regional Cancer Center, Medical Coll., Trivandrum 695011, Kerala, India**
**Indian J Cancer; 18(4):268-270 1981**

The homing patterns of purified lymphocytes of oral cancer patients were compared to those of lymphocytes obtained from healthy controls. Lymphocytes from both groups were isolated and tagged with 51 Chromium in vitro, then injected into mice. Four hr later, radioactivity in liver and spleen was determined and compared. The homing pattern of lymphocytes obtained from oral cancer patients was drastically different from that of lymphocytes obtained from controls. The ratio of radioactivity in the liver/spleen of controls was 31.5:1, while that of oral cancer patients was 10.5:1. These differences could be eliminated if lymphocytes from cancer patients were incubated at 37 C for 24 hr, presumably destroying a cell surface abnormality. These results are compatible with the presence of circulating antigens or antigen-anti body complexes in the peripheral blood of cancer patients. (6 Refs)

### 57. EFFECT OF RADIOTHERAPY ON THE IMMUNOCOMPETENCE IN PATIENTS WITH BRONCHOGENIC CARCINOMA AND LARYNGEAL CANCER.

**Oshitani T**
**Dept. Radiology, Kobe Univ. Sch. Medicine, Kobe, Japan**
**Nippon Igaku Hoshasen Gakkai Zasshi; 41(9):873-886 1981**

We evaluated the immunocompetence of 80 patients with bronchogenic carcinoma and 17 patients with laryngeal cancer undergoing radiotherapy, using collectively many types of immunological parameters. In patients with bronchogenic carcinoma, no significant difference was seen with PHA and PPD skin tests, but the reactivity of PHA skin tests gradually decreased in the course of treatment. It was assumed that radiotherapy might not interfere with the recognition of antigen. Lymphocyte blastoid transformations with PHA, ConA and PWM were all inhibited significantly. Since these three mitogens can stimulate the different groups of lymphocyte, the inhibition to the proliferative function of lymphocyte due to radiotherapy would seem to cover a wide area, including T and B lymphocyte. Concerning the comparative radiosensitivity of T and B lymphocyte, no significant result was obtained. However, in the dose of 20Gy the percentage of T lymphocyte decreased, while the percentage of B lymphocyte increased. The percentage of early rosettes, one subset of T cell, decreased more sensitively than that of T cell, but there was no significant difference. The percentage of IgGFcR(+)T cell, considered a part of cytotoxic T cell or suppressor T cell, decreased significantly in the dose of 20 Gy, but returned to a high value in the dose of 40Gy. As the helper T cell can be considered radioresistant, it has been suggested that radiotherapy might give the host an immunological enhancement against tumor if a certain suitable method is used. Immunocompetence of cases in Stage III, which was significantly high before treatment, decreased to the same level as those in Stage IV according to the treatment. In patients with laryngeal cancer, lymphocyte counts and reactivity of PHA skin tests were not influenced by radiotherapy, and then reactivity of PPD skin tests and lymphocyte blastoid transformations with PHA and ConA tended to increase instead. Those results seemed to come mainly from the removal of inhibition to the immune system due to tumor, so we hope the estimate of immunocompetence can bring us influential information for judgement of the time of recurrence. (Author abstract) (64 Refs) (In JPN)

## 58. INDICES OF CELLULAR IMMUNITY IN LUNG CANCER PATIENTS AFTER SURGICAL AND COMBINED TREATMENT.

**Kharchenko VP, Sutiagin AG, Danilova TS, Pankina VKh**
**Res. Roentgenoradiological Inst., Moscow, USSR**
**Sov Med; (10):33-36 1981**

The effect of treatment on the state of cellular immunity was studied in 100 lun g cancer patients (96 men, 4 women; 40-69 yr old). Among these patients, 29 underwent surgery alone, 34 received preoperative radiotherapy (300 rads, 5x/wk, total dose 3,600 rads), and 37 received postoperative radiotherapy (dosage and schedule as above). Immunological status was assessed prior to, during, and 6 and 12 mo after the treatment. Prior to the treatment, the lung cancer patients showed significant decrease of the indices of blast-transformation reaction (33% vs 50% in healthy controls), the number of rosette-forming cells (38% vs 53.9%), and absolute count of T-lymphocytes (733 vs 1,202). A more intensive normalization of the indices of cellular immunity was observed in the patients subjected to surgery alone or to surgery with preoperative radiotherapy. (8 Refs) (In RUS)

## 59. SHORT-TERM EFFECT OF IRRADIATION ON THE PERIPHERAL LYMPHOCYTE POPULATIONS IN PATIENTS TREATED WITH HIGH-ENERGY PHOTON BEAM.

**Fekete B, Petranyi J, Reischl G, Gyarmathy L**
**Natl. Inst. Tuberculosis and Pulmonology, P. O. Box 1, H-1529 Budapest, Hungary**
**Strahlentherapie; 157(8):542-543 1981**

Changes in lymphocyte populations were studied in 22 patients with testicular cancer before and after a single 2-Gy dose of high-energy photon beam. Absolute lymphocyte counts as well as total T-and active T cells markedly decreased immediately after irradiation, whereas no significant alterations in Fc receptor-bearing lymphocytes and B cell counts were produced. Recovery of lymphocyte populations was relatively rapid, reaching pre-irradiation values by 24 hours. (Author abstract) (14 Refs)

## 60. CANCER IMMUNOTHERAPY: SOME CRITICAL COMMENTS REGARDING IMMUNOLOGICAL MONITORING.

**Amery WK**
**Janssen Pharmaceutica N.V., B-2340 Beerse, Belgium**
**Int J Immunopharmacol; 3(4):339-348 1981**

Determination of pretreatment immune status and measurement of drug-related changes in immune response during cancer chemotherapy with levemisole (LV) are discussed. Prior cancer sensitization may be a prerequisite for successful LV treatment and can be determined by various direct and indirect in vivo and in vitro tests. Detection of pretreatment defects in immunologic expression is discussed under the following headings: energy and lymphocytes, monocytes/macrophages, B-lymphocytes, miscellaneous humoral factors, tumor load, suppressor cells, in vitro modulation of functions, and mononuclear cell enumeration. Delayed-type hypersensitivity skin reactions, phytohemagglutinin-induced blast formation, Fc-receptor-bearing lymphocytes, mixed lymphocyte culture reactivity, 'null' cell numbers, and monocyte chemotaxis may show changes during LV therapy and may serve as prognostic indicators. LV may enhance tumor-specific cell-mediated immunity and prolong the presence of high levels of antitumor membrane IgG antibodies in sera of patients receivin g tumor vaccines. Exogenous factors that could interfere with desirable immune changes, including surgery, radiotherapy and chemotherapy, are discussed. Timing of LV therapy is discussed in relation to timing of conventional treatment and to the last dose of LV; duration of LV treatment; time as a chronobiological variable; and time as related to delayed-type hypersensitivity skin testing. (57 Refs)

## 61. COMPARISON OF THE IN VITRO EFFECT OF BIGUANIDES AND SULFONYLUREAS ON INSULIN BINDING TO ITS RECEPTORS IN TARGET CELLS.

**Vigneri R, Pezzino V, Wong KY, Goldfine ID**
**Cattedra di Endocrinologia e Patologia Costituzionale, Universita di Catania, Ospedale Garibaldi, 95123 Catania, Italy**
**J Clin Endocrinol Metab; 54(1):95-100 1982**

The in vitro effects of two biguanides (phenformin and metformin) and four sulfonylureas (tolbutamide, glyburide, gliclazide, and glisolamide) on insulin binding to its receptors were studied in four cultured cell lines: human skin fibroblasts, IM-9 lymphoblasts, MCF-7 human mammary carcinoma, and H35 rat hepatoma. After a 24-hr preincubation with maximal stimulatory concentrations of phenformin, specific [125I]insulin binding to its receptors in the four different cell lines was increased over control by 67.2 +-17.0%, 101.3 +-11.5%, 65.1 +-8.0 and , and 44.0 +-12.1%, respectively (mean +- SE). Phenformin was effective in IM-9 cells that were down-regulated by unlabeled insulin, and the effect of phenformin on insulin binding was not affected by inhibition of protein synthesis with cycloheximide. In concert with this observation, Scatchard plots indicated that phenformin increased the insulin receptor's affinity rather than the number of insulin-binding sites on IM-9 cells. Metformin was also effective in significantly enhancing insulin binding in both IM-9 and MCF-7 cells. In contrast to the effects of biguanides, none of the four sulfonylureas tested had any significant influence on insulin binding to any of the four cell lines. These agents were also ineffective in IM-9 cells that were down-regulated by insulin. Therefore, these studies suggest that: (1) in vitro, biguanides enhance insulin binding to its receptors in a variety of cell types; (2) this effect of biguanides doesn't depend on new receptor synthesis; it is a result of changes in the affinity of the insulin receptor; and (3) in contrast to the biguanides, the sulfonylureas do not have a major direct effect on insulin binding to its receptors in most cell types. (Author abstract) (19 Refs)

## 62. IMMUNOLOGIC PARAMETERS OF CHILDREN WITH ACUTE LEUKOSIS AFTER CESSATION OF POLYCHEMOTHERAPY UNDER REPEATED IMMUNOSTIMULATION WITH INTRADERMAL B.C.G.

**Blau HJ, Eggers G, Kruse H, Schulz M, Grulich M**
**Kinderklinik des Bereiches Medizin, Wilhelm-Pieck-Universitat Rostock, Rembrandtstr. 16/17, DDR-2500 Rostock, E. Germany**
**Arch Geschwulstforsch; 52(2):123-128 1982**

Immunologic parameters were measured in children with acute leukosis during immunostimulation with BCG after cessation of polychemotherapy. Fourteen patients, including 11 with acute lymphoblastic leukemia (ALL) and 3 with acute myeloblastic leukemia (AML) began immunostimulant therapy 6 wk after cessation of a 3-yr course of intensive polychemotherapy. BCG (0.05 ml) was injected id 2x/yr up to 5 yr and once/yr thereafter. BCG vaccination produced significant increases in peripheral-blood counts of lymphocytes (4,466 x 10(9)/liter before BCG vaccination to 7,240 x 10(9)/liter 6 wk after the third vaccination) and cells forming E-rosettes (48.5 +-21.1%

before BCG treatment to 53.2 +-13.0% 6 wk after the third vaccination). Three out of 24 skin tests showed positive tuberculin reaction. A control group of patients with AML who received polychemotherapy but no BCG treatments showed no such increases. No relapse occurred in 14 patients receiving BCG during 1-3 yr observation. Among controls 19/30 were alive and 15/30 were in stable remission after an av 4 yr. Results suggest beneficial effects of BCG vaccination for patients with ALL or AML, but the patient sample was too small too draw definite conclusions. (11 Refs)

### 63. CONCOMITANT INDUCTION OF CYTOTOXIC AND SUPPRESSOR CELLS: MODULATION BY THEOPHYLLINE.

**Rola-Pleszczynski M, Lieu H**

**Div. Immunology, Dept. Pediatrics, Universite de Sherbrooke, Sherbrooke, Quebec J1H 5N4, Canada**

**Cell Immunol; 65(1):13-19 1981**

Previous studies in man have shown that T cells with suppressor activity were mainly found among a subset bearing Fc receptors for IgG (T gamma). Recently, we found that virus-induced cytotoxic effector cells were also found predominantly among T gamma cells. In the present studies, we present evidence that similar, possibly overlapping T-cell populations can mediate both suppressor and cytotoxic activities when sensitized in vitro with virus-infected cells. In fact, both activities are found within the positively selected T gamma subset, but not in the T gamma-depleted population; both activities are abolished by irradiation but not by treatment with mitomycin C; a 1-hr exposition to theophylline at the onset of sensitization enhances both cytotoxic and suppressor activities. The data suggest that development of antiviral cell-mediated immune responses in vivo may also be accompanied by a concurrent induction of nonspecific suppressor cells. Such suppressor activity may play a role in the depressed cellular immune responsiveness which is associated with several systemic virus infections. (Author abstract) (25 Refs)

### 64. THE IN VITRO EFFECT OF A CALF THYMUS EXTRACT (THYMOSTIMULIN) ON THE IMMUNOLOGIC PARAMETERS OF PATIENTS WITH UNTREATED HODGKIN'S DISEASE.

**Martelli MF, Velardi A, Rambotti P, Cernetti C, Bracaglia AM, Ballatori E, Davis S**

**(c/o Davis) Oncology/Clinical Hematology, Veterans Admin. Medical Center, East Orange, NJ, 07019**

**Cancer; 49(2):245-250 1982**

The in vitro effect of a calf thymus extract, thymostimulin (TP-1), on the E-rosette-forming capacity and on the PHA blastogenic response of peripheral blood lymphocytes was evaluated in 20 patients with untreated Hodgkin's disease. The mean percentage of lymphocytes forming E rosettes increased in patients from 44.2% to 57.5% (p less than 0.005). The mean PHA stimulation index rose with all three concentrations tested, but returned to the normal range only with the highest PHA concentration (60 u/ml). An increase in the immune parameters was greatest in those patients who presented with decreased E-rosetting cells or total lymphocyte counts or whose disease was Stage III or IV or of mixed cellular histology. (Author abstract) (30 Refs)

### 65. ADCC OF CULTURED HUMAN MELANOMA CELLS: ANALYSIS WITH MONOCLONAL ANTIBODIES TO HUMAN MELANOMA-ASSOCIATED ANTIGENS.

**Imai K, Ng AK, Glassy MC, Ferrone S**

**Dept. Molecular Immunology, Scripps Clinic and Res. Foundation, La Jolla, CA**

**Scand J Immunol; 14(4):369-377 1981**

Four monoclonal antibodies to human melanoma-associated antigens (MAA) were found to be able to mediate specific cell-dependent lysis (ADCC) of cultured human melanoma cells. The extent of specific lysis of melanoma cells was influenced by the effector to target cell ratio, the amount of antibody added to the reaction mixture, and the incubation time. Cultured melanoma cells treated for 16 hr with puromycin or cycloheximide (final concentration, 1.0 ug/ml) displayed increased susceptibility to ADCC even though the cell surface expression of MAA was not changed. On the other hand, treatment of melanoma cells with tunicamycin (final concentration, 1.0 ug/ml) reduced the expression of MAA but did not affect susceptibility to ADCC. These findings suggest that other properties of the target cell membrane besides antigen density play a role in the outcome of ADCC reaction. (Author abstract) (16 Refs)

## OTHER RELATED STUDIES

### 66. CELLULAR INTERACTIONS MODULATING HOST RESISTANCE TO TUMOURS.

**Baldwin RW, Byers VS, Hannant D, Jones JA, Pimm MV, Price MR**

**Cancer Res. Campaign Lab., Univ. Nottingham, University Park, Nottingham NG7 2RD, England**

**Recent Results Cancer Res; 80:338-345 1982**

Active specific immunotherapy of carcinogen-induced rat tumors can be effected using vaccines containing tumor cells admixed with bacterial vaccines such as BCG and C parvum. The nature of the tumor antigen preparation is important, the most effective immunogen being viable tumor cells whose growth is controlled by responses generated by the bacterial agent in the vaccine. Soluble tumor antigen preparations are usually ineffective due to the preferential induction of suppressor lymphocyte responses in normal hosts. In comparison, removal of suppressor precursors by cyclophosphamide treatment of animals leads to the development of tumor immunity following immunization with soluble antigen preparations. One component of the immune rejection response involves the generation of non-specific effector cells. This type of response can also be induced by administering chemical hypersensitizing agents so as to localize tumor deposits. This approach has proved highly effective in treating the guinea pig line 10 hepatoma by intralesional injection of alkylcatechols. These compounds are highly potent hypersensitizers, being the active constituents of the poison ivy/oak (urushiol oil), and localize in tumor cell membranes. (Author abstract) (17 Refs)

## 67. HYBRIDOMA MONOCLONAL ANTIBODY: USE IN DEFINING SURFACE ANTIGENS ON HUMAN LUNG CARCINOMA CELLS.

**Kassi M, Saxton RE, Holmes EC, Burk MW, Morton DL, Bonnard, Alexander P, Ferrone S, Ivanyi P, Nathanson SD, Pious D, Embleton MJ**

**54-140 CHS, UCLA Sch. Medicine, Los Angeles, CA, 90024**

**Transplant Proc; 13(4):1942-1946 1981**

Surface antigens on UCLA-SO-P3, the squamous cell lung carcinoma cell line derived from a 53-yr-old man, were compared with those on PL3, the autologous lymphoblast line obtained from the same patient. Using the autologous cell lines, two hybridomas were selected which secrete monoclonal antibodies that bind antigenic determinants present at high density on the carcinoma cells but not on the paired lymphoblastoid cells. The two cloned hybridomas, designated 169D4 and 169F3, were grown as ascites tumors in mineral oil-primed BALB/c mice. The two binding curves obtained by titration of hybridoma cells with P3 and PL3 target cells were compared. An end-point titer greater than 1:100,000 for both antibodies to the P3 carcinoma but only 1/:10 to PL3 for the 169D4 monoclonal antibody and 1:100 for 169F3 was revealed. The shapes of these antibody binding curves showed that the antigenic determinants recognized by the two monoclonal antibodies were present at high density on the P3 carcinoma but at low density or absent from the PL3. The immunoglobulin isotype of both 169D4 and 169F3 monoclonal antibodies was identified as IgM. The two monoclonal antibodies were tested for binding to 12 carcinoma cell lines, 9 melanoma, 2 sarcoma, 4 lymphoblast, and 1 human embryonic. Among the cell lines tested, only the lung carcinoma P3 and the colon carcinoma HT29 expressed detectable levels of 169D4 surface antigen. 169F3 monoclonal antibody recognized an epitope present on every human tumor cell line and on human embryo cells, but not on the lymphoblastoid cell lines. (6 Refs)

## 68. MONOCLONAL ANTIBODIES AGAINST SURFACE ANTIGENS OF LARYNGEAL CARCINOMA CELLS.

**Zenner HP**

**Universitatsklinik und Poliklinik fur Hals-, Nasen-, und Ohrenkranke, Kopfklinikum Wurzburg, D-8700 Wurzburg, W. Germany**

**Arch Otorhinolaryngol; 233(2):161-172 1981**

Production of monoclonal antibodies against laryngeal carcinoma (LC) cells is reported. BALB/c mice were immunized with LC cells of line HLaC78 (1 x 10(6)-5 x 10(7) cells x 2 at a 6-wk interval) or with cell membranes (CM) from LC cells. Spleen cells were obtained 3 days after the second injection. Spleen cells were fused with mouse myeloma 653 cells to form antibody-producing cells capable of proliferation. A total of 1,882 clones of spleen cells were developed, including 1,102 from mice immunized with CM and 780 from mice immunized with intact cells (IC). Antibodies that bound to intact LC were produced by 73 clones, all from IC-immunized mice. Antibody from one clone was identified which bound malignant target cells, including two types of LC and two types of salivary gland tumor cells, but which did not bind normal fibrocytes, lymphocytes, or other normal human cell types, or nonhuman cells. The antibody, produced by hybridoma clone 1g6, was an IgG. Diagnostic potential of the IgG is described. (32 Refs) (In GER)

## 69. INTERFERON: IMMUNOBIOLOGY AND CLINICAL SIGNIFICANCE.

**Stiehm ER, Kronenberg LH, Rosenblatt HM, Bryson Y, Merigan TC**

**Dept. Pediatrics, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA, 90024**

**Ann Intern Med; 96(1):80-93 1982**

Interferons are proteins elaborated by infected cells that protect noninfected cells from viral infection. These proteins produce a temporary 'antiviral state' by altering nucleotide metabolism and cytoplasmic enzyme induction. Interferons appear early after viral infection locally and systematically to limit spread of viral infection; they also affect cell differentiation, growth, surface antigen expression, morphologic findings, and immunoregulation. Several human disorders have diminished interferon production. Newborns have normal interferon alpha but deficient interferon gamma production. Infants with congenital infections may also have defects in interferon production. Immunosuppressed patients receiving transplants (marrow, heart, or kidney) have diminished interferon production, particularly immediately after transplant. Deficiencies of interferon have also been noted in Down's syndrome, cellular immunodeficiencies, uremia, malnutrition, and hematopoietic malignancy. Leukocyte interferon has been of therapeutic value in herpes zoster infections, in patients with cancer, and in patients with hepatitis B infection. Interferon has not been proved to help children with congenital cytomegalovirus or rubella. Interferon can shrink lymphoid tumors, particularly non-Hodgkin's lymphoma. (Author abstract) (160 Refs)

## 70. GAMMA (IMMUNE) INTERFERON PRODUCTION BY LEUKOCYTES FROM A PATIENT WITH A TG CELL PROLIFERATIVE DISEASE.

**Hooks JJ, Haynes BF, Detrick-Hooks B, Diehl LF, Gerrard TL, Fauci AS**

**NIDR, NIH, Building 10, Room 2B19, Bethesda, MD, 20205**

**Blood; 59(1):198-201 1982**

We report a patient with a disease characterized by proliferation of T cells with Fc receptors for IgG (TG). However, unlike lymphoid cells from normal individuals or from patients with other lymphoid malignancies, the patient's lymphocytes spontaneously produced gamma interferon (IFN-gamma) in vitro. The peripheral lymphocytes consisted of 95% TG cells, which exhibited the morphological characteristics of T-cell chronic lymphocytic leukemia (CLL) and were normal on cytochemical and chromosome analysis. The majority of TG cells were OKT3+, OKT8+, and OKT4-, 3A1-. These cells failed to express suppressor cell activity and displayed depressed levels of natural killer activity, but mediated antibody-dependent cell-mediated cytotoxicity. The spontaneous production of IFN-gamma by human peripheral lymphoid cells as demonstrated in this study may serve as a probe for studying the relationship between IFN-gamma and the proliferation of human T-cell subsets. (Author abstract) (16 Refs)

## 71. T-CELL GROWTH FACTOR-MEDIATED PROLIFERATION OF LYMPHOCYTES FROM A T-CHRONIC LYMPHOCYTIC LEUKAEMIA PATIENT LACKING MITOGEN AND ALLOANTIGEN RESPONSIVENESS.

**De Vries JE, Vyth FA, Mendelsohn J**
**Div. Immunology, The Netherlands Cancer Inst., Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands**
**Clin Exp Immunol; 43(2):302-310 1981**

Peripheral blood lymphocytes (PBL) of chronic lymphocytic leukemia of T cell origin (T-CLL), which were unresponsive to mitogens and had negligible stimulator and responder capacities in mixed lymphocyte cultures (MLC), were induced to proliferate by human T cell growth factors (TCGF). Long-term T-CLL PBL cultures were obtained in the presence of TCGF. T-CLL PBL obtained from a female patient (30 yr old) showed no 3H-thymidine (3HTdR) incorporation when stimulated with various concentrations of phytohemagglutinin (PHA), Concanavalin A, or pokeweed mitogen. The T-CLL PBL exhibited greatly reduced responder and inducer capacities (12% and 14% that of normal sheep RBC rosette-forming cells, respectively). TCGF-1 had the strongest growth-promoting activity and was used as a standard (1.0 growth-promoting unit). TCGF-1,-2, and-3 contained 0.52, 0.29, and 0.33 growth-promoting units, respectively. PHA stimulated proliferation of T-CLL cells in the presence of TCGF-1. Both TCGF-3 and-4 also induced and maintained T-CLL PBL proliferation in the presence of PHA, but at considerably lower rates than those produced in the presence of TCGF-1 and-2. In MLC, addition of TCGF-4 resulted in a four-fold increase in 3H-TdR incorporation in T-CLL PBL after stimulation with lymphocytes from a normal donor (C). Lymphocytes from donor C showed an 80-fold increase in 3H-Td R incorporation when cultured with T-CLL PBL in the presence of TCGF-4. The results indicated that the lack of response to mitogens and alloantigens of the T-CLL PBL can be attributed to the failure of these cells to produce TCGF upon activation. (36 Refs)

## 72. INCREASED RESPONSES TO LYMPHOKINES ARE CORRELATED WITH PRELEUKEMIA IN MICE INOCULATED WITH MOLONEY LEUKEMIA VIRUS.

**Lee JC, Ihle JN**
**Biological Carcinogenesis Program, NCI-Frederick Cancer Res. Facility, Frederick, MD, 21701**
**Proc Natl Acad Sci USA; 78(12):7712-7716 1981**

In various mouse strains, inoculation with Moloney leukemia virus results in the establishment of an acute viremia which in most cases is followed by the induction of leukemia. Also associated with the viremia is the development of a chronic cellular immune response detectable in vitro by the ability of viral proteins to induce splenic lymphocyte proliferation. Previous studies have demonstrated that, in the absence of this cellular immune response, leukemia does not develop irrespective of whether viremia is present. In vitro proliferative responses to antigens involve the nonspecific response of various subpopulations of lymphocytes to lymphokines produced by antigen-specific Thy 1+, Lyt 1+,2-lymphocytes. The studies presented here concern the effects of a chronic immune response in viremic mice on the frequency of lymphocytes capable of responding to lymphokines in vitro. The data demonstrate that the number of responsive lymphocytes is increased 30-to 100-fold in preleukemic mice and that such increases are dependent upon the induction of an immune response in viremic mice. The role of this altered immune response in leukemia is discussed. (Author abstract) (18 Refs)

## 73. MECHANISMS CONTROLLING TCGF PRODUCTION BY CLONED SUBLINES OF EL-4 AZGR IN RESPONSE TO STIMULATION BY ANTI-THY-1 ANTIBODY.

**Shimizu S, Smith RT, Norcross MA, Maino VC**
**(c/o Smith) Dept. Pathology, Univ. Florida Coll. Medicine, Box J-275, Gainesville, FL, 32610**
**J Immunol; 128(1):296-301 1982**

The effect of xenogeneic anti-Thy-1 antibody on T cell growth factor (TCGF) production by T lymphoma cell lines has been examined as a model system for T cell activation. EL-4 G12 (a cloned subline of the producer EL-4 azgr cell line) produced TCGF when stimulated by a high concentration of anti-Thy-1, but none was induced by low concentrations of anti-Thy-1. Large amounts of TCGF were produced when these cells were cultured with Fc-receptor positive (FcR+) accessory cells. TCGF production by EL-4 G12 showed dose response kinetics similar to TCGF production by anti-Thy-1 stimulated purified normal spleen T cells. Goat anti-rabbit IgG (GaRIG) and Protein A substituted for this accessory helper effect, but neither FcR+ cells nor Protein A worked when (Fab')2 anti-Thy-1 was used instead of IgG anti-Thy-1. Anti-T-200 monoclonal antibody inhibited anti-Thy-1-induced TCGF production by EL-4 G12 and accessory cells. Phorbol myristic acetate and lymphocyte-activating factor also substituted in part for the accessory cell help. The data suggest there are at least two different accessory cell help mechanisms in anti-Thy-1-induced TCGF production, anti-Thy-1-bound membrane aggregation either by GaRIG, Protein A or FcR, and a LAF-dependent mechanism. (Author abstract) (29 Refs)

## 74. NEUTROPHIL MIGRATION INHIBITION FACTOR FROM T LYMPHOCYTES (NIF-T): SELECTIVE REMOVAL OF BIOLOGIC ACTIVITY BY HUMAN PERIPHERAL BLOOD NEUTROPHILS, MYELOCYTIC LEUKEMIA CELLS, AND DIFFERENTIATED HL-60 CELLS.

**Weisbart RH, Lusis AJ, Chan G, Billing R, Ashman RF, Golde DW**
**Dept. Medicine, Div. Rheumatology, Veterans Admin. Medical Center, 16111 Plummer St., Sepulveda, CA, 91343**
**J Immunol; 128(1):457-462 1982**

Neutrophil migration inhibition factor from T lymphocytes (NIF-T) is a newly recognized mediator that may regulate neutrophil function. In this report we show that normal and leukemic human peripheral blood neutrophils selectively removed NIF-T activity from conditioned medium. Removal of NIF-T activity was similar at 37 C and 4 C, neutrophil supernatants did not destroy NIF-T activity, and purified neutrophil plasma membranes removed NIF-T activity at zero degrees in contrast to the microsomal fraction of neutrophils, suggesting that membrane binding was responsible for neutrophil removal of NIF-T activity. The specificity of the removal of NIF-T activity by human neutrophils was indicated by the absence of detectable removal by human peripheral blood monocytes and alveolar macrophages and by neutrophils from other species. Moreover, cells from patients with acute and chronic myelocytic leukemia removed measurable NIF-T activity, whereas cells from a patient with acute myelomonocytic leukemia did not. In contrast to other human lymphoid and myeloid cell lines, only the human promyeloblast cell line, HL-60, removed NIF-T activity. Uninduced HL-60 cells removed only about 7% of the NIF-T activity removed by neutrophils. Differentiation of HL-60 cells by exposure to dimethyl sulfoxide, however, enhanced the removal capacity for NIF-T to that of peripheral blood neutrophils, and differentiated HL-60 cells responded to NIF-T in the migration assay. The responsiveness of differentiated

HL-60 cells to NIF-T was, however, markedly impaired. Monocytes differentiated from HL-60 by 12-O-tetradecanoylphorbol-13-acetate did not remove measurable NIF-T activity. These results suggest human neutrophils and neutrophil precursors express specific binding sites for NIF-T. (Author abstract) (37 Refs)

## 75. T-CELL GROWTH FACTOR (INTERLEUKIN 2) CONTROL OF T-LYMPHOCYTE PROLIFERATION: POSSIBLE INVOLVEMENT IN LEUKEMOGENESIS.

**Gillis S, Mertelsmann R, Moore MA**
**Basic Immunology Program, Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104**
**Transplant Proc; 13(4):1884-1890 1981**

Isolation of murine and human leukemic T-cell lines that produce exceptionally high quantities of interleukin 2 (IL-2), and screening of freshly isolated patient-derived human leukemic blasts for IL-2 production and response capabilities, are described. An IL-2 microassay was used to screen fractions of biochemically manipulated, conditioned medium for the capacity to promote sustained in vitro proliferation of murine cytotoxic T-lymphocytes. Two leukemic cell lines, murine LBRM-33 and human Jurkat-FHCRC, produced large quantities of IL-2 upon stimulation with phytohemagglutinin (PHA). Both of the cell lines bear conventional T-cell markers and phenotypic markers indicative of immature cell type. Analysis of leukemic blast cell response of mononuclear blood cells from patients with various leukemias revealed consistent IL-2 production and response patterns. All patients who exhibited high levels of deoxynucleotidyl transferase (TdT) in leukemic blood cells showed a small proliferation increase in response to PHA stimulation but produced exceptionally high levels of IL-2. The response to added purified human IL-2 and PHA was atypical in most patients, in that incorporation of 3H-thymidine decreased in the majority of TdT+ leukemias when compared to PHA-stimulated proliferation. Such a finding was in marked contrast to results obtained with normal lymphocytes. IL-2 production and use responses and TdT expression in leukemic cells are discussed. (17 Refs)

## 76. NATURAL KILLER CELLS - SURVEILLANCE MECHANISM AGAINST ABNORMAL CELLS.

**Klessling R, Karre K**
**Institutionen for tumorbiologi, Karolinska institutet, Stockholm, Sweden**
**Lakartidningen; 78(46):4131-4134 1981**

Recent studies on natural killer (NK) cells are reviewed. NK cells stem from the bone marrow, and their maturation is not dependent on the thymus. They are probably lymphocytes, but their relationship to T-cells is unknown: they have low concentrations of certain T-cell markers on their membranes. Unlike B-cells, they have no membrane-bound immunoglobulins. The NK cell function is not reduced in experimental animals and humans with inborn immune defects in the T- and B-cell systems. Since the NK cells have no 'immunological memory', they can be activated nonspecifically by interferon and interferon-producing agents. However, the activation does not lead to the clonal proliferation of the NK cells. The NK cells also produce interferon themselves after recognizing and being bound to certain types of tumor cells. The findings indicate that the NK activity is of greatest significance during the initial stage of the immune reaction. The cells of tumor metastases are characterized by considerably reduced sensitivity to NK cells com pared with those of the primary tumor. (4 Refs) (In SWE)

## 77. NATURAL KILLER ACTIVITY OF GUT MUCOSAL LYMPHOID CELLS IN MICE.

**Tagliabue A, Luini W, Soldatesch! D, Boraschi D**
**Sclavo Res. Center, Via Fiorentina 1, I-53100 Siena, Italy**
**Eur J Immunol; 11(11):919-922 1981**

Intraepithelial lymphoid cells (IEL) obtained from the mucosa of mouse small intestine were tested for natural killer (NK) activity in a 20-hr 51Cr-release assay against YAC-1 and RL male 1 tumor cells. It was found that IEL possess a strong NK activity, higher than spleen cells, whereas lymphocytes from Peyer's patches (PPL) did not show any NK activity. The cytotoxic activity of IEL could be boosted by interferon (IFN-beta) treatment, but no NK activity could be induced in PPL by in vitro IFN-beta treatment. The characteristics of the NK effector cells present in the mouse intestine strictly resemble those of NK cells in the spleen. In fact, intestinal NK activity is not affected by depletion of adherent cells and only partially reduced by anti-Thy-1.2 antibodies plus complement. Moreover, the age dependency of NK cytotoxicity is identical for IEL and spleen. Finally, NK-insensitive target cells are not lysed by IEL. (Author abstract) (17 Refs)

## 78. EFFECTOR CELL SENSITIVITY TO SUGAR MOIETIES. I. INHIBITION OF HUMAN NATURAL KILLER CELL ACTIVITY BY MONOSACCHARIDES.

**Ades EW, Hinson A, Decker JM**
**Dept. Basic and Clinical Immunology and Microbiology, Medical Univ. South Carolina, Charleston, SC, 29425**
**Immunobiology; 160(2):248-258 1981**

Human natural killer (NK) cells recognize multiple target antigens. The ligands (antigens) involved in the effector-target cell interaction have not been extensively identified. In the present study, assays of NK activity in the presence of a panel of monosaccharides demonstrated inhibition of cytolysis in a dose-response fashion. We proposed that NK cell activity involves the recognition of carbohydrate structures on target cells via receptors on the effector cell surface. (Author abstract) (23 Refs)

## 79. ANTITUMOR IMMUNITY IN B-LYMPHOCYTE-DEPRIVED MICE. II. IN VITRO STUDIES.

**Brodt P, Gordon J**
**Dept. Surgery, Div. Surgical Res., McGill Univ., Donner Building, 740 Docteur Penfield Ave., Montreal, Quebec H3A 1A4, Canada**
**Cell Immunol; 65(1):20-32 1981**

In a previous publication, we reported that B-lymphocyte-deprived mice possess a heightened in vivo resistance to a methylcholanthrene-induced syngeneic fibrosarcoma. The present in vitro study has disclosed that spleens of such mice possess a significantly higher cytotoxic activity against the same tumor compared to normal rabbit globulin-injected control animals, and that this increase cannot be accounted for by the mere elimination of B lymphocytes. The cell mediating this response was found to be a natural-killer-like cell on the basis of its organ distribution, its full activation without immunization, its target specificity shown directly and by cold target inhibition experiments, and by its surface markers. It is suggested that this increased activity, which does not appear to decline with age, may be responsible for the heightened in vivo antitumor resistance of T mice. (Author abstract) (32 Refs)

## 80. A T-CELL LINE DERIVED FROM NORMAL HUMAN CORD LEUKOCYTES BY CO-CULTURING WITH HUMAN LEUKEMIC T-CELLS.

Miyoshi I, Kubonishi I, Yoshimoto S, Shiraishi Y
Dept. Medicine, Kochi Medical Sch., Oko-cho, Nankoku-shi, Kochi-ken 781-51, Japan
Gan; 72(6):978-981 1981

A unique T-cell line, MT-2, was established from normal human cord leukocytes of a male infant by co-culturing with leukemic T-cells from a female patient with adult T-cell leukemia. MT-2 cells expressed receptors for sheep erythrocytes and complement and were reactive with anti-T-cell and anti-Ia sera. They were negative for Fc receptors, surface immunoglobulin, and Epstein-Barr virus nuclear antigen. Chromosomally, the MT-2 line was male and most cells were shown to have a normal diploid karyotype. The cultured cells were tumorigenic when transplanted into immunosuppressed newborn hamsters. (Author abstract) (11 Refs)

## 81. TRANSFORMATION OF NORMAL HUMAN CORD LYMPHOCYTES BY CO-CULTIVATION WITH A LETHALLY IRRADIATED HUMAN T-CELL LINE CARRYING TYPE C VIRUS PARTICLES.

Miyoshi I, Yoshimoto S, Taguchi H, Ohtsuki Y, Kubonishi I, Shiraishi Y, Akagi T
Dept. Anatomy, Kochi Medical Sch., Oko-cho, Nankoku-shi, Kochi-ken 781-51, Japan
Gan; 72(6):997-998 1981

Normal human cord WBC were co-cultured with lethally irradiated MT-2 cells to produce a T-cell line of cord WBC origin which harbored type C virus particles and adult T-cell leukemia-associated antigens (ATLA). On the 11th day of culture, 1 x 10(6) lethally x-irradiated (6,000 R) MT-2 cells were added to two of four dishes of cord WBC. Control cultures included two dishes of irradiated MT-2 cells without cord WBC and two dishes of cord WBC alone. All cultures were incubated at 37 C in a humidified 7.5% CO2 atmosphere. Two wk after co-culture, scattered foci of cell aggregates were observed on the sheets of macrophages. Continuous growth of cells developed in two of the co-cultured dishes, and this cell line, designated Ok, was maintained in culture for 3 mo. The Ok line consisted of mostly immature lymphoid cells with multinucleate giant cells. Sixty-six percent of the Ok cells formed spontaneous rosettes with neuraminidase-treated sheep RBC. Most of the Ok cells were positive for Leu-1 and OK11, but negative for Leu-2a and Leu-3a. None of the 145 Ok cells studied contained a Y chromosome; 41/46 cells had a 46,XX karyotype. Electron microscopy revealed many type C virus particles in the extracellular spaces. Most of the Ok cells were positive for ATLA when reacted with ATL patient's sera. The cultured cells gave a positive reaction with five sera from ATL patients but not with five sera from normal control individuals. These findings suggest that the type C virus was apparently transmitted from the MT-2 cells to the cord lymphocytes during co-cultivation. (8 Refs)

## 82. CHARACTERIZATION OF A BONE MARROW CELL LINE TRANSFORMED BY ABELSON'S MURINE LEUKEMIA VIRUS.

Pinter A, Borzsonyi M
Orszagos Kozegeszsegugyi Intezet, Budapest, Hungary
Magy Onkol; 25(4):217-226 1981

Development of transformed cell line (Gr 17) was observed after infection of a long-term bone marrow cell culture from BALB/c mice with Abelson's murine leukemia virus (strain P 160) (A-MuLV). According to their phenotype, the Gr 17 cells corresponded to the early maturation form of B lymphoid cells (pre-B lymphoblasts). The results of the tests for alpha-naphthylacetate esterase, Hb, phagocytosis, and membrane surface Ig were negative, but cytoplasmic IgM was found. In contrast to the hitherto described cell lines obtained by transformation with A-MuLV, hypodiploid chromosome set and the presence of metacentric chromosome due to translocation were observed. Development of thymus-independent generalized lymphoma was observed after transplantation of Gr 17 cells (2 x 10(7) cells iv) in 4-6-wk-old male and female BALB/c mice. The take rates were 9/10 in the females and 8/10 in the males. The mean latent periods were 41 days in the females and 50 days in the males. Typical Abelson's tumors were induced by the virus produced by the cell line in newborn BALB/c mice. (27 Refs) (In HUN)

## 83. ESTABLISHMENT OF B-LYMPHOBLASTOID CELL LINES FROM MAREK'S DISEASE VIRUS-INDUCED TUMORS IN TURKEYS.

Nazerian K, Elmubarak A, Sharma JM
Regional Poultry Res. Lab., U. S. Dept. Agriculture, 3606 East Mount Hope Road, East Lansing, MI, 48823
Int J Cancer; 29(1):63-68 1982

Four lymphoblastoid cell lines were established from tumors of turkeys inoculated with high doses of the GA strain of Marek's disease virus (MDV). Unlike other MD lymphoblastoid cell lines of chicken origin, these MDV transformed turkey lines appear to be B lymphocytes and produce immunoglobulin. Growth characteristics of these cell lines are slightly different; however, they all produce low levels of MDV-specific antigen and carry the complete genome of the virus as determined by virus rescue in the chicken or in duck embryo fibroblast cultures. These cell lines are pathogenic for chickens and produce virus-induced MD lesions. All four lines are free of the herpesvirus of turkeys, reticuloendotheliosis virus, and three lines are also free of avian leukosis virus. They all have typical normal turkey chromosomes and are positive for Marek's disease tumor-associated surface antigen. (Author abstract) (24 Refs)



☆ U. S. GOVERNMENT PRINTING OFFICE : 1982—361-847/119

# AUTHOR INDEX WITH CITATION NUMBERS


Abe I. 3
Abell CA. 16
Ades EW. 78
Adler WH. 13
Akagi T. 81
Alexander P. 67
Amagasaki T. 7
Amery WK. 60
Andersson LC. 48
Artacho MC. 5
Ashman RF. 74
Bach FH. 42
Bach JF. 20
Baldwin RW. 66
Ballatori E. 64
Bankhurst AD. 14
Bankhurst AD. 27
Bennett CE. 18
Bergman Y. 34
Billing R. 74
Blau HJ. 62
Bonavida B. 37
Bonnard. 67
Bonnard GD. 33
Boraschi D. 77
Borzsonyi M. 82
Boucheix C. 9
Boue DR. 46
Bracaglia AM. 64
Bricas E. 20
Brodt P. 79
Bryson Y. 69
Bubenik J. 49
Bubenikova D. 49
Burk MW. 67
Burton RC. 41
Byers VS. 66
Cernetti C. 64
Chan G. 74
Chang-xue Z. 28
Check IJ. 25
Cheresh DA. 17
Chiba Y. 3
Christen D. 36
Cohen DA. 38
Danilova TS. 58
Dardenne M. 20
Davis S. 64
De Vries JE. 71
DeMeester TR. 25
Decker JM. 78
Delia D. 45
Detrick-Hooks B. 70
Diehl LF. 70
Dierich MP. 15
Distasio JA. 17
Dokhelar MC. 50
Eggers G. 62
Ehlen T. 15
Elias L. 27
Elmubarak A. 83
Embleton MJ. 67
Fauci AS. 70
Fekete B. 59
Felix E. 21
Ferrone S. 42
Ferrone S. 65
Ferrone S. 67
Finale Y. 50
Finn O. 34
Forster HK. 36
Froelich CJ. 14
Galili N. 6
Galili U. 6
Gartemann A. 19
Gastinel LN. 20
Gerrard TL. 70
Gillis S. 42
Gillis S. 75
Giorgi JV. 41
Giraudo Conesa. 26
Glass EJ. 16
Glassman AB. 18
Glassy MC. 65
Golde DW. 74
Goldfine ID. 61
Goldstein G. 45
Goldstein IJ. 51
Golomb HM. 25
Gordon I. 18
Gordon J. 79
Goronzy J. 39
Greaves MF. 45
Green M. 31
Grulich M. 62
Gudat FG. 36
Gutterman JU. 24
Gyarmathy L. 59
Hammerling GJ. 39
Hannant D. 66
Hata Y. 29
Haynes BF. 70
Heacock EH. 28
Hersh EM. 24
Hijmans W. 8
Hilz H. 19
Hinson A. 78
Hirose M. 35
Hockley AB. 44
Hoffman GC. 4
Holmes EC. 67
Hooks JJ. 70
Hunter RL. 25
Ihle JN. 72
Ikeda S. 7
Imai K. 65
Ishii Y. 47
Ivanyi P. 67
Iwamoto T. 10
Izumi A. 55
Jakobiec FA. 10
Jandlova T. 49
Jansen J. 8
Jones EH. 44
Jones JA. 66
Kamada R. 11
Kamihira S. 7
Kanayama H. 55
Kaplan AM. 38
Kaplan JH. 52
Karre K. 76
Karrison T. 25
Kasai M. 67
Katz S. 21
Kawamura S. 3
Kay AB. 16
Kenney DM. 43
Kersey JH. 46
Kharchenko VP. 58
Kiessling R. 76
Kikuchi K. 47
Kinoshita K. 7
Klein PJ. 30
Knowles DM. 10
Koga S. 55
Kojima K. 11
Koshiba H. 47
Kotani H. 1
Kronenberg LH. 69
Kruse H. 62
Kuang Y. 23
Kubonishi I. 80
Kubonishi I. 81
Kukita K. 29
Kung P. 45
Lastovicka J. 49
Lawler SD. 44
LeBien TW. 46
Lee JC. 72
Levy JP. 40
Levy R. 34
Li C. 23
Lieu H. 63
Lilly F. 40
Lindner A. 53
Lischner HW. 12
Lockwood SH. 52
Longmire J. 27
Lopez DM. 17
Lozzio BB. 31
Lozzio CB. 31
Luini W. 77
Lusis AJ. 74
Lynch M. 26
Maddox DE. 51
Madgar I. 53
Maeta M. 55
Maino VC. 73
Maldonado J. 5
Mannick JA. 28
Many M. 53
Marelli O. 37
Marie JP. 9
Martelli MF. 64
Martin WJ. 37
Martin WJ. 42
Matsumoto M. 11
Meijer CJ. 8

Mendelsohn J 71
Merigan TC 69
Mertelsmann R 75
Meruelo D 42
Minato K 35
Minowada J 45
Miyoshi I 80
Miyoshi I 81
Moore MA 75
Morgan J 24
Morgat JL 20
Moroz C 53
Morton DL 67
Murphy SG 24
Mussel HH 15
Nathanson SD 67
Nazerian K 83
Neville ME 12
Newman RA 30
Newman RA 45
Ng AK 65
Norcross MA 73
Obrecht JP 36
Ohtsuki Y 81
Onikul SR 28
Or R 6
Osaki Y 55
Oshitani T 57
Pajdak E 54
Pandolfi F 33
Pankina VKh 58
Parkman R 43
Parola AH 52
Pasqualini RS 26
Peiper SC 2
Perrine S 43
Perrot JY 9
Petranyi J 59
Pezzino V 61
Pieskus J 22
Pimm MV 66
Pinter A 82
Pious D 67
Pituch-Noworols 54
Plata F 40
Pleau JM 20
Polliack A 6
Price MR 66
Pujato D 26
Quesada J 24
Rambotti P 64
Ramirez G 5
Reischl G 59
Remold-O'Donnel 43
Rola-Pleszczyns 63
Rosen FS 43
Rosenblatt HM 69
Rosenfeld C 9
Sadauskas P 22
Saitoh A 3
Salem P 50
Sardi J 26
Sasaki A 20
Sasaki F 29
Sato K 29
Savage RA 4
Saxena QB 13
Saxena RK 13
Saxton RE 67
Schilder RJ 17
Schuit HR 8
Schulz KD 30
Schulz M 62
Schwoch G 19
Scott D 41
Sharma JM 83
Shibata S 51
Shimizu N 55
Shimizu S 73
Shimoyama M 35
Shiraishi Y 80
Shiraishi Y 81
Silverman MA 17
Slease RB 33
Smith RT 73
Soldateschi D 77
Stass SA 2
Stewart D 24
Stiehm ER 69
Strong DM 33
Sun Y 23
Surovas V 22
Sutherland DR 45
Sutiagin AG 58
Tagliabue A 77
Taguchi H 81
Takagi K 11
Taki T 11
Tamosiunas V 22
Teodorescu A 21
Teodorescu M 21
Terhorst C 32
Testa U 50
Tetaud C 50
Tilkin AF 40
Tobinai K 35
Tsuchida S 3
Tursz T 50
Twig S 53
Uchino J 29
Uhr JW 37
Une Y 29
Uzgiris EE 52
Vainchenker W 50
Valenzuela R 4
Van Agthoven A 32
Van Nieuwkoop J 8
Vardiman J 25
Velardi A 64
Vierbuchen M 30
Vigneri R 61
Vijayakumar T 56
Vogel CL 17
Vyth FA 71
Wang BS 28
Warner NL 14
Warner NL 41
Weber W 19
Weisbart RH 74
Weyand C 39
Wielckens K 19
Wilbur SM 37
Witten M 18
Wong KY 61
Wurz H 30
Wust CJ 31
Yamada Y 7
Yamaya T 3
Yoshida Y 3
Yoshimoto S 80
Yoshimoto S 81
Young TH 28
Zander A 24
Zarling JM 42
Zenner HP 68
Zhang G 23
Zittoun J 9
Zittoun R 9

**U.S. DEPARTMENT OF COMMERCE**
**National Technical Information Service**
5285 Port Royal Road
Springfield, Va. 22161

OFFICIAL BUSINESS

Penalty for Private Use, $300

**PRINTED MATTER**

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF COMMERCE
COM-211

THIRD CLASS
BULK RATE

U.S.MAIL

CB-17

**CANCERGRAMS** are distributed for the International Cancer Research Data Bank (ICRDB) by the National Technical Information Service (NTIS). **CANCERGRAMS** are available from NTIS on a standing order basis at $2 each for North American Continent addressees and $3 each for other addressees. An NTIS deposit account is required. For a list of subject categories or other information, please write to:

Subscription Section
National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161

**NOTICE OF MAILING CHANGE**

☐ Check here if you wish to discontinue receiving this publication.

☐ Check here if your address has changed and you wish to continue receiving this publication. (Be sure to furnish your complete address including zip code.)

Tear off cover with address label still affixed and send to:

Computer Support Center
ICRDB Program
IIT Research Institute
10 West 35th Street
Chicago IL. 60616

CB 17/82/07

NCI/ICRDB/CB17 82/07

PB82-931807

ICRDB

# CANCERGRAM

# IMMUNOBIOLOGY AND CANCER

## Identification and Characterization of Immune Cells

SERIES CB17 No. 82/07

JULY, 1982

This Cancergram is a service of the INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM of the U.S. National Cancer Institute. Every few weeks, an updated Cancergram containing abstracts of selected cancer-related articles recently published in more than 3000 journals, and dealing with the topic indicated by the above title, is sent to researchers working in this area. These researchers are identified on the basis of the description of their current research project that has been submitted to the ICRDB Program, directly or via granting agencies.

This Cancergram is prepared by the Cancer Information Dissemination and Analysis Center (CIDAC) for Virology, Immunology, and Biology. *If this Cancergram is useful and valuable, please send your comments to the CIDAC address below, since future editions depend on user satisfaction and user needs:*

CIDAC FOR VIROLOGY, IMMUNOLOGY, AND BIOLOGY
SCIENCE INFORMATION SERVICES
FRANKLIN INSTITUTE RESEARCH LABORATORIES
20TH AND RACE STREETS
PHILADELPHIA, PA 19103

NEWARK PUBLIC LIBRARY

AUG 24 1982

U. S. GOVT. PUBS.
DEPOSITORY 376

DID YOU KNOW?? EACH CANCERLIT SEARCH THAT PROVIDES YOU WITH USEFUL DATA CAN BE STORED IN THE COMPUTER FOR AUTOMATIC SEARCHING OF NEW DATA EACH MONTH. ASK YOUR LIBRARIAN ABOUT AUTOMATIC SELECTIVE DISSEMINATION OF INFORMATION (AUTO-SDT).

*In this issue:*


- CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS..... 1-15
- DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS..... 16-30
- LYMPHOCYTE AND DIFFERENTIATION ANTIGENS..... 31-43
- CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION..... 44-57
- EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS..... 58-63
- OTHER RELATED STUDIES..... 64-75


U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service • National Institutes of Health • National Cancer Institute

HE 20.3173/2:

## CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS

### 1. THE LEUKEMIC CELL.

Catovsky D
MRC Leukaemia Unit, Royal Postgraduate Medical Sch., London, England
Methods Hematol 2: 281 pp., 1981.

New objective criteria for diagnosis and classification of leukemia have permitted better characterization of various forms of leukemia, facilitated recognition of new disease entities, contributed to understanding of the natural history of leukemia, and led to improved management of the disease. Rapid advances in technology have allowed better description of cellular events in hemopoietic malignancies while making it more difficult for specialists to keep up with new developments. Techniques currently available for the study of leukemic cells are presented in sufficient detail to make the techniques of practical value. A general review is presented. Individual topics discussed include cytochemistry in classification of leukemias, bone marrow histology, ultrastructure of the leukemic cell, membrane markers in leukemia, chromosomes in leukemia and lymphoma (with emphasis on methodology), terminal transferase, the clonal culture in vitro of leukemic cells, and glucocorticoid receptors. Discussion includes methods, clinical and scientific principles, and the significance of results. Problems that may be encountered are described and methods of resolution presented. (892 Refs)

### 2. OVERVIEW: THE LEUKEMIC CELL.

Catovsky D
MRC Leukemia Unit, Royal Postgraduate Medical Sch., London, England
Methods Hematol; 2:1-28 1981

Leukemias are classified generally as acute or chronic and myeloid or lymphoid. Within the broad categories are many individual disease entities that differ in prognosis and response to therapy. Recognition of specific forms requires consideration of morphology, cytochemistry, histology, membrane markers, enzyme assays, chromosome analysis, cloning of individual cell lines, and glucocorticoid receptors. (171 Refs)

### 3. MEMBRANE MARKERS IN LEUKEMIA.

Janossy G
Dept. Immunology, Royal Free Hosp., London, England
Methods Hematol; 2:129-183 1981

Analysis of membrane markers to determine the type and heterogeneity of leukemic cells is presented. Detection of surface markers can be accomplished using conventional antibodies or monoclonal antibodies. Methods of preparation of both types are detailed. Uses of immunological reagents (antisera and RBC reagents for rosette tests) are described. Interpretation of observations and relationships between leukemic and normal cells are discussed. (171 Refs)

### 4. IMMUNOLOGIC CLASSIFICATION OF LYMPHOCYTIC LEUKEMIAS BASED ON MONOCLONAL ANTIBODY-DEFINED CELL SURFACE ANTIGENS.

Schroff RW, Foon KA, Billing RJ, Fahey JL
Medical Immunology Res. Lab., Dept. Microbiology and Immunology, Univ. California, Los Angeles, CA, 90024
Blood; 59(2):207-215 1982

A panel of monoclonal antibodies reactive with normal lymphocyte subsets was used to classify cases of lymphocytic leukemia on the basis of cell surface antigen expression. The antibodies employed were commercially available and included a common framework HLA-DR antibody, two pan-T antibodies (Leu-1 and OKT-3), and antibodies defining cytotoxic/suppressor (Leu-2 and OKT-8) and helper/inducer (Leu-3 and OKT-4) subpopulations of normal T lymphocytes. Cases of ALL could be subgrouped into non-T non-B, pre-T and T-ALL on the basis of reactivity with HLA-DR, Leu-1, and OKT-3 antibodies. Leukemic cells from patients with T-cell CLL could be divided into Leu-2/OKT-8 reactive and Leu-3/OKT-4 reactive subpopulations, as well as a subgroup in which the majority of cells were unreactive with either of these antibodies. With the exception of one individual, all Sezary cell leukemias expressed a phenotypic pattern similar to that of the Leu-3 subgroup of T-CLL. Malignancies of B-cell lineage (B-CLL, prolymphocytic leukemia, and lymphosarcoma) that were examined were reactive with both the HLA-DR and Leu-1 antibodies. On the contrary, normal B lymphocytes and lymphoid cell lines of B-cell origin did not express surface antigens recognized by the Leu-1 antibody. (Author abstract) (56 Refs)

### 5. HAIRY CELL LEUKEMIA. A REVIEW.

Sanchez Rodriguez A, Jimenez Lopez A
Departamento de Patologia Medica, Facultad de Medicina, Universidad de Salamanca, Salamanca, Spain
Rev Clin Esp; 163(1):9-12 1981

Hairy cell leukemia (HCL) was reviewed under the following headings: clinical signs, peripheral blood, bone marrow, spleen, hairy leukocyte and its markers, ultrastructural study, origin of hairy leukocytes, and treatment. At present, splenectomy is the best treatment, with survival time of 10 yr in one case. (71 Refs) (In SPA)

### 6. UNUSUAL INTRACYTOPLASMIC IMMUNOGLOBULIN INCLUSIONS IN CHRONIC LYMPHOCYTIC LEUKAEMIA.

Guglielmi P, Preud'Homme JL, Gourdin MF, Reyes F, Daniel MT
INSERM U 108, Hopital Saint Louis, 75475 Paris Cedex 10, France
Br J Haematol; 50(1):123-134 1982

Unusual intracytoplasmic immunoglobulin inclusions were found by immunofluorescence in three patients with chronic lymphocytic leukemia. The inclusions contained the same immunoglobulin chains as those detected on the plasma membrane, except for delta chains which were expressed on the cell surface and not in the cytoplasmic inclusions. The cytoplasmic staining persisted throughout culture for 8 or more days. An initial study of patient number one's cells showed that the inclusions contained only mu chains, and kappa chains gradually became apparent after in vitro culture. In a second study, the fresh lymphocytes contained both mu and kappa chains. Initially, biosynthetic experiments showed production of mu chains which polymerized in the cytoplasm and were not secreted. Subsequently there was synthesis of heavy and light chains

which assembled into monomeric subunits that were retained and secretion of free light chains. The apparent mol wt of these immunoglobulin chains was larger than that of their secretory counterparts. Immunoelectronmicroscopy revealed cytoplasmic mu chains in strands of endoplasmic reticulum. In the two other patients, immunofluorescence displayed unusual staining patterns of bright networks in perinuclear areas. (Au thor abstract) (31 Refs)

## 7. THE PRESENCE OF MONOCLONAL CYTOPLASMIC IMMUNOGLOBULINS IN LEUKEMIC B CELLS FROM PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA.

Han T, Ozer H, Bloom M, Sagawa K, Minowada J
Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Blood; 59(2):435-438 1982

It has generally been assumed that CLL B cells do not contain cytoplasmic immunoglobulin (CyIg), although these cells express surface membrane immunoglobulin (SmIg). The present study, in which SmIg and CyIg determinations were performed simultaneously using leukemic B cells from 20 patients with CLL, demonstrates that CyIg staining was detectable in each CLL cell population examined and that the intensity of cytoplasmic immunofluorescent staining in each instance was moderate to strong. Both SmIg and CyIg light chain determinations indicated monoclonality in all 20 cases. The heavy chain class of SmIg and CyIg in each CLL cell population was not uniformly comparable, however. The majority (15 cases) of CLL B cells contained mu heavy chain CyIg and mu and delta heavy chain CyIg was demonstrated in the remaining six cases. In contrast, the SmIg phenotype appeared heterogenous with both gamma and alpha chain determinants found associated with mu or mu and delta chains on the same leukemic cell populations. This apparent polyclonal SmIg staining pattern was most likely due to nonspecific adsorption of the patient's own serum Ig by Fc receptors on CLL B cells. It is concluded that the great majority of CLL B cells contain detectable CyIg and that CyIg determination is superior so SmIg phenotyping in documenting the monoclonality of CLL. (Author abstract) (12 Refs)

## 8. PHENOTYPIC CHANGES IN A CASE OF BLAST CRISIS OF CML: CHARACTERIZATION BY TDT, CYTOCHEMISTRY, AND CYTOGENETICS.

Paletta E, Schwarzmeier JD
First Medical Dept., Univ. Vienna Medical Sch., Lazarettgasse 14, A-1090 Vienna, Austria
Scand J Haematol; 27(4):241-246 1981

Phenotypic changes in blast crisis of a case of Philadelphia chromosome (Ph1)-positive chronic myelogenous leukemia were characterized by serial terminal transferase (TdT) determinations simultaneously related to cytochemical and cytogenetic data. At the onset of the blast crisis, 90% of the blast cells were acid phosphatase-positive (focal pattern), Ph1-positive, lymphoid cells. The TdT activity amounted to 29 units/10(8) mononuclear cells in the peripheral blood and to 57 units/10(8) mononuclear cells in the bone marrow. Therapy with vincristine and prednisone caused the elimination of the TdT-positive cell population. Four mo later, there was an increase in TdT-negative, myeloid blasts which was brought under control with busulfan. Cytogenetic analysis of the myeloid blasts still revealed Ph1 positivity in 100% of the metaphases examined and the lack of additional chromosomal abnormalities. A second relapse was again dominated by TdT-containing cells with the 46,XX,Ph1 karyotype. This time, the patient failed to achieve remission with vincristine and prednisone. Even though the TdT activity was markedly decreased, the lymphoid blast count remained elevated and the cells showed resistance to further therapy. This failure of morphology, cytochemistry as well as cytogenetics to distinguish between the individual phenotypes emerging during the course of blast crisis of CML characterized the TdT as a cell marker of important diagnostic and therapeutically prognostic value. (Author abstract) (17 Refs)

## 9. ABNORMAL GLUCOCORTICOID RECEPTOR IN ACUTE LEUKEMIA CELLS.

McCaffrey R, Lillquist A, Bell R
Section Medical Oncology, Boston Univ. Medical Center, 75 East Newton St., Boston, MA, 02218
Blood; 59(2):393-400 1982

In normal tissues, 3H-triamcinolone acetonide (3H-TA) labeled glucocorticoid receptors can be resolved into two components by DEAE chromatography: peak I elutes at 0.04 M salt and peak II at 0.22 M salt. By glycerol gradient centrifugation, peak I is 3.5S and peak II is 8.5S. Peak I binds to DNA, while peak II does not. Blast cell 3H-TA-binding macromolecules in 27 of 62 cases of acute leukemia had DEAE binding characteristics identical to those of normal tissues; the remaining 35 cases were abnormal. In these cases there was either a single DEAE species eluting in the peak I area (30 cases) or multiple low-amplitude peaks eluting across the entire gradient (5 cases). The abnormal single peak material failed to bind to DNA in five cases (of 5 studied), whereas peak I material from five cases (of 5 studied), showing normal peak I-peak II ratios, bound normally to DNA. In three cases (of 3 studied), the abnormal single peak material had a S value of 2-2.5S, whereas in five cases with normal peak I-peak II ratios, the S values were a 3.5S and 8.5S, respectively. We hypothesize that those leukemias with abnormal binding characteristics cannot respond to glucocorticoid therapy. (Author abstract) (27 Refs)

## 10. GLUCOCORTICOID RECEPTOR AND IN VITRO SENSITIVITY TO STEROID HORMONES IN HUMAN LYMPHOPROLIFERATIVE DISEASES AND MYELOID LEUKEMIA.

Nanni P, Nicoletti G, Prodi G, Galli MC, De Giovanni C, Grilli S, Lollini PL, Gobbi M, Cavo M, Tura S
Istituto di Cancerologia, Universita di Bologna, via S. Giacomo 14, 40126 Bologna, Italy
Cancer; 49(4):623-632 1982

The glucocorticoid receptor (GR) quantitation by a whole-cell assay and/or cytosol technique and the in vitro sensitivity to steroids have been assessed in peripheral blood cells from normal donors and patients with chronic lymphatic leukemia (CLL), acute lymphoblastic leukemia (ALL), lymphosarcoma cell leukemia (LSCL), acute nonlymphatic leukemia (ANLL), and chronic myeloid leukemia (CML). Within the lymphoproliferative diseases, ALL cells exhibited the highest GR concentration (regardless of the method used) and the highest in vitro inhibition of spontaneous [3H]thymidine ([3H]TdR) uptake by glucocorticoids. A significant relationship between GR concentration (whole-cell assay) and in vitro sensitivity to dexamethasone was also found. On the contrary, CLL cells presented the highest sensitivity to glucocorticoids in PHA-stimulated cell cultures. Cells from the only two ALL patients who did not undergo a remission after glucocorticoid-inclusive chemotherapy had both the lowest in vitro sensitivity to dexamethasone and the lowest GR concentration with whole-cell assay. Con-

cerning myeloid leukemia, ANLL patients had GR concentrations slightly higher than those found in the ALL group but exhibited the lowest degree of inhibition of spontaneous [3H]TdR uptake by dexamethasone (stimulatory effects occurred in some cases). CML cells exhibited an inhibition degree by in vitro glucocorticoids significantly higher than that of ANLL cells but not different from that of lymphoproliferative diseases. No clear relationship among GR pattern, in vitro cell sensitivity to glucocorticoids, and clinicohematologic parameters was observed in myeloid leukemia-bearing patients. (Author abstract) (38 Refs)

## 11. CORRELATION BETWEEN VARIANT TRANSLOCATION AND EXPRESSION OF IMMUNOGLOBULIN LIGHT CHAINS IN BURKITT'S LYMPHOMAS AND LEUKEMIAS.

Lenoir G, Preud'homme JL, Bernheim A, Berger R
Programme des Mecanismes de la Cancerogenese, Centre international de Recherche sur le Cancer, 150, cours Albert-Thomas, 69372 Lyon Cedex 2, France
C R Acad Sci [III] (Paris); 293(8):427-429 1981

Expression of immunoglobulins (IG) in Burkitt's lymphomas (19 lines) and leukemias (1 line) are discussed in relation to observed chromosome abnormalities. Of the 19 lymphoma lines, 12 were non-endemic and 7 did not contain the Epstein Barr virus. IG light chains produced varied according to the type of translocation. In 17/18 cases with translocation t(8;14), the light chains of surface and cytoplasmic IG were type kappa (9 cases) or type gamma (8 cases). The cells of patient 18 did not express any detectable light chains. In 3/5 cases of translocation t(2;8), the light chains were type kappa with light chain expression in 1/3; the two other cell lines exhibited a pre-B phenotype. Of six cases with translocation t(8;22), IG with gamma chains were found in 5 and a pre-B phenotype in the sixth. IgM, sometimes associated with IgD, was found in 17/19 cell lines; two cell lines were characterized by monoclonal gamma IgG (translocation t(8;14) in one case and t(8;22) in the other). The results indicated the existence of a relationship between translocations t(2;8) and t(8;22) and light chain expression: kappa in the case of t(2;8) and gamma in the case of t(8;22). (12 Refs) (In FRE)

## 12. IMMUNOLOGICAL SUBSETS IN HUMAN B-CELL LYMPHOMAS.

Godal T, Lindmo T, Marton PF, Landaas TO, Langholm R, Hoie J, Abrahamsen AF
Lab. Immunology, Norwegian Radium Hosp., Montebello, Oslo 3, Norway
Scand J Immunol; 14(5):481-492 1981

Fifty human B-cell lymphomas have been studied with regard to surface markers (surface immunoglobulins (sIg) and complement receptors (CR)), capping of sIg, and relative amounts of sIg by single-cell flow cytometry. The results show that these lymphomas can be subdivided into distinct immunological subsets. Whereas one histological subgroup (lymphocytic) consisted of only one immunological subtype, others were heterogeneous with regard to immunological subtypes. This was most striking in nodular lymphomas of germinal center cell origin (centroblastic/centrocytic). Our studies provide further evidence for the existence of a large number of subsets in the B-cell compartment of the immune system. sIgD was only found in association with sIgM. The relative amounts of sIgD varied, especially in nodular lymphomas. A discrepancy between capping of sIgM and sIgD was also found in some lymphomas belonging to this group. These findings together with other observations suggest that sIgD plays a role in B-cell maturation and differentiation events taking place in germinal centers and becomes lost during this process. A close association was found between the presence of CR and capping of sIgM but not capping of sIgD or sIgG. Nodular lymphomas expressing sIgG only, lacked CR. These findings suggest that CR may become lost during maturation and differentiation processes also taking place in germinal centers. Lymphoplasmacytoid lymphomas, which show morphological evidence of differentiation towards plasma cells, could be subdivided into three immunological subsets, indicating that plasma cell maturation may take place from different subsets of B cells. (Author abstract) (39 Refs)

## 13. IMMUNO-HISTOLOGICAL ANALYSIS OF BONE MARROW INVOLVEMENT IN LYMPHOPROLIFERATIVE DISORDERS.

Pizzolo G, Chilosi M, Cetto GL, Fiore-Donati L, Janossy G
Sezione di Enatologia, Policlinico di Borgo Roma, 37134 Verona VR, Italy
Br J Haematol; 50(1):95-100 1982

Cryostat sections from bone marrow biopsies submerged in gum-sucrose solution and snap-frozen can be stained with various antisera to detect both the membrane and cytoplasmic antigens on normal and malignant populations in their tissue environments. This technique seems to be the method of choice to analyze the degree of BM involvement in cases of non-Hodgkin's lymphoma where conventional histology provides equivocal results. The uniform expression of only one type of light chain in B lymphoma and the analysis of the T cell infiltrate in T-CLL using monoclonal antibodies is demonstrated. (Author abstrac t) (9 Refs)

## 14. CHARACTERIZATION OF NORMAL AND MALIGNANT HUMAN LYMPHOID CELL POPULATIONS.

Ford RJ
Dept. Pathology, Univ. Texas M.D. Anderson Hosp. and Tumor Inst., Houston, TX
Cancer Bull; 33(6):255-260 1981

Characterization of human lymphoid cell populations with both conventional cell membrane markers and monoclonal antibodies is reviewed. The most reliable human T-cell marker is the sheep red blood cell rosette assay, usually performed with neuraminidase-treated sheep RBC. The cell-surface immunoglobulin receptor is the most reliable human B-cell marker; others include the membrane receptor for Epstein-Barr virus and the mouse RBC membrane receptor. Monocytes and macrophages may be identified and separated by means of the phagocytosis of latex particles; in addition, enzymes such as alpha-naphthylacetate esterase are relatively specific for the monocyte/macrophage system when present in a diffuse cytoplasmic staining pattern. Hybridoma technology has given rise to the use of mouse monoclonal antibodies for identifying various types of human lymphocytes. Panels of monoclonal antibodies with defined specificities will probably make conventional cell markers obsolete in the near future. Conventional immunologic markers for a number of neoplastic lymphoid cells, including T- and B-cell lymphomas and leukemias and histiocytic lymphomas, are discussed. Recent studies concerning the use of monoclonal antibodies for differentiation of lymphoma and lymphocytic leukemia subtypes are described. (38 Refs)

### 15. LYMPHOMATOID PAPULOSIS: A CUTANEOUS T-CELL PSEUDOLYMPHOMA.

Burg G, Hoffmann-Fezer G, Nikolowski J, Schmoeckel C, Braun-Falco O, Stunkel K
Frauenlobstr. 9, D-8000 Munchen 2, W. Germany
Acta Derm Venereol (Stockh); 61(6):491-496 1981

It was the purpose of this study to further define the nature of the dermal infiltrates in lymphomatoid papulosis (LP) by means of enzyme cytochemistry (acid phosphatase and esterase), immunology (rosetting techniques, immunoperoxidase technique on cryostat sections), and by semithin and ultrathin sections. The studies performed on biopsy samples with clinically and histologically typical LP indicated that most lymphoid cells display markers for T-lymphocytes, which were helper T-cells in the one case studied with monoclonal antibodies. Regarding the typical benign self-involutive clinical course, LT is considered to be a cutaneous pseudolymphoma of T-cell type. (Author abstract) (24 Refs)

## DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS

### 16. MEMBRANE-BOUND AND SECRETED IGA CONTAIN STRUCTURALLY DIFFERENT ALPHA-CHAINS.

Sitia R, Kikutani H, Rubartelli A, Bushkin Y, Stavnezer J, Hammerling U
Dept. Immunology, Servizio P.C.P.C., Ospedale S. Martino, Viale Benedetto XV, 10 16132 Genoa, Italy
J Immunol; 128(2):712-716 1982

Three different forms of alpha-chains are synthesized by BFO.3 and 615.2, two cloned cell lines derived from the murine B lymphoma I.29. The three forms of alpha-chains differ in size, pI, cellular location, and rate of turnover. They were identified by means of lactoperoxidase-catalyzed radioiodination, internal 14C or 35S labeling, and immunofluorescence techniques as membrane-bound(alpham), secreted (alphas), and intracellular (alphaic) proteins. Comparison of immunoglobulin products of the two lymphoma lines with those of a hybridoma cell line, Id 150, which secretes IgA of the I.29 idiotype but lacks membrane IgA, confirmed the assignments of alpham, alphas, and alphaic. Results of biosynthetic labeling of BFO/3, 615.2, and Id 150 in the presence and absence of tunicamycin suggest that the difference in mol wt and charge observed between alpham and alphas can be attributed to differences in primary amino acid structure rather than different degrees of glycosylation. (Author abstract) (28 Refs)

### 17. CLONAL ANALYSIS OF B AND T CELL RESPONSES TO IA ANTIGENS. III. CHARACTERIZATION OF 12 XENOGENEIC ANTI-IDIOTYPIC ANTISERA TO A.TH-DERIVED ANTI-I-AK AND ANTI-I-EK MONOCLONAL ANTIBODIES.

Devaux C, Pierres M
(c/o Pierres), Centre d'Immunologie INSERM-CNRS de Marseille-Luminy, Case 906, 13283 Marseille Cedex 9, France
J Immunol; 128(2):751-757 1982

We attempted to evaluate the idiotypic diversity of A.TH anti-Iak antibody responses by characterizing 12 xenogeneic anti-idiotypic antisera (anti-Id) produced against individual or pools of A.TH-derived anti-I-Ak or anti-I-Ek monoclonal antibodies (mAb). Sensitive cross-idiotype binding assays with 12 anti-Id and 35 125I-labeled A.TH-derived anti-Iak mAb demonstrated that one anti-Id bound only its homologous ligand, whereas 11 others detected recurrent idiotypic specificities on their homologous and various heterologous ligands. Each unlabeled homologous ligand was able to inhibit the idiotype binding of the corresponding anti-Id antiserum. However, in the majority of the anti-Id systems analyzed, no inhibition of homologous idiotype binding was observed with large excess of heterologous ligands. Such discrepancies between cross-idiotype binding and competitive inhibition of idiotype binding assays indicated either recognition by the anti-Id of cross-idiotypic determinants on heterologous ligands with low affinity, or the existence of two types of anti-Id antibodies in these sera: a dominant one directed at private idiotypic specificities only expressed on the homologous ligand, and another detecting recurrent idiotypic specificities on various heterologous ligands. In most of the idiotypic systems analyzed in this study there was no apparent correlation between the fine antigenic specificities of the various anti-Iak mAb precipitated by a given anti-Id. However, the cross-idiotype binding pattern of three anti-Id suggested a fraction of idiotypic determinants might be shared between some or all of the anti-Ia.1 and anti-Ia.7 mAb, respectively. The binding of radiolabeled anti-Iak mAb to spleen cells could be inhibited by most anti-Id, suggesting the idiotypic determinants recognized by these anti-Id were in proximity of the anti-Iak mAb combining site. The data support the conclusion that A.TH anti-Iak mAb may express individual (Idl) and recurrent (IdX) idiotypic specificities that can be recognized by xenogeneic anti-Id antisera. Such reagents represent, therefore, appropriate probes to analyze the cellular receptors for Ia antigens and the idiotype-anti-idiotype regulation of allospecific immunity. (Author abstract) (42 Refs)

### 18. DEFECTIVE STEROID RECEPTORS IN A GLUCOCORTICOID RESISTANT CLONE OF A HUMAN LEUKEMIC CELL LINE.

Harmon JM, Schmidt TJ, Thompson EB
Lab. Biochemistry, Div. Cancer Biology and Diagnosis, NCI, NIH, Bethesda, MD, 20205
Adv Exp Med Biol; 138:301-313 1982

Several glucocorticoid resistant mutants derived from the steroid sensitive human leukemic cell line CEM-C7 were isolated, characterized, and studied. The mutants contain receptors capable of binding glucocorticoids. Results indicate that mere presence of steroid binding activity, even in cells or tissues which generally express steroid regulated functions, does not guarantee the existence of a functional, steroid responsive, pathway. More detailed analyses of glucocorticoid receptors from clinical material is required to establish a relationship between receptors and clinical response. (30 Refs)

### 19. STRUCTURAL SIMILARITY OF MOLYBDATE-STABILIZED STEROID RECEPTORS IN HUMAN BREAST TUMORS, UTERI AND LEUKOCYTES.

Niu EM, Neal RM, Pierce VK, Sherman MR
(c/o Sherman) Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
J Steroid Biochem; 15:1-10 1981

Effects of molybdate on the apparent quantity and/or structure of the cytosol receptors for progestins and estrogens in human breast tumors, progestins in benign and malignant uterine endometrium, and glucocorticoids in normal lymphocytes and leukemic cells were studied. Estrogen receptors (ER) were labeled with [6,7-3H]-estradiol, glucocorticoid receptors with [6,7-3H]-triamcinolone acetonide (TA), progestin receptors

(PR) with [17alpha-methyl-3H]-promegestone (R5020), and serum corticoid-binding globulin with [4-14C]-cortisol. For kinetic studies, the control solutions (-Mo) were made 30 milli (m)M in KCl, so that they had the same conductivity as those containing 20 mM Na2MoO4 (+Mo). In the -Mo samples labeled with R5020, the specific binding was max between 1 and 2.5 hr, but declined to 54% of this value by 6.5 hr. In the +Mo samples labeled with either lower or higher progestin concentrations, at lea st 92% of the max binding persisted after 6.5 hr; indicating that molybdate inhibits many but not all of the receptor-degrading processes in breast tumor (BT) cytosols. Results of gel filtration of PR and ER in BT and uterine specimens indicated that all of these receptors appear to exist in the same discrete form in hypotonic +Mo buffers, regardless of the class of steroid, species, tissue, or state of health or malignancy. Steroid-binding specificity and ultracentrifugal analyses of molybdate stabilized receptors showed that the significant inhibition of progestin binding to PR by the synthetic glucocorticoid TA paralleled the inhibition detected in unfractionated +Mo cytosol. Comparison of molecular parameters indicated mol wt of approx 310,000, an axial ratio of 11, and that the molecular architecture of receptors is highly conserved in a wide range of mammalian tissues. (55 Refs)

## 20. INSULIN RECEPTORS ON HUMAN LYMPHOID LINES OF B-CELL ORIGIN.

**Aman P, Lundin G, Hall K, Klein G**

**Dept. Tumor Biology, Karolinska Institut, S-104 01 Stockholm, Sweden**

**Cell Immunol; 65(2):307-316 1981**

Human lymphoid lines derived from normal or neoplastic B cells were assayed for insulin binding. 125I-Labeled insulin was allowed to bind to cells. Bound radioactivity which was inhibited with unlabeled insulin was regarded as specific binding. Among 46 lines tested, 43 bound more insulin than normal peripheral B lymphocytes. The majority of the lines resembled activated lymphocytes, with regard to their insulin binding. More mature cells represented by EBV-transformed lines of normal origin, bound more insulin than the less differentiated Burkitt lymphoma lines. However, even the latter bound significantly more insulin than peripheral blood lymphocytes. (Author abstract) (35 Refs)

## 21. ASSAYS FOR TRANSFERRIN AND TRANSFERRIN RECEPTORS IN TUMOUR AND OTHER MOUSE TISSUES.

**De Abrew S**

**Cancer Inst., 481 Little Lonsdale St., Melbourne 3000, Australia**

**Int J Nucl Med Biol; 8(4):217-221 1981**

Measurements of the binding of 125I human transferrin to single cell preparations from mouse tissues indicated that the av number of transferrin receptors per cell was about 10(5) for RILQ lymphoma cells, approx 5 x 10(4) for the spleen population, less than 5 x 10(3) for cells from the thymus, and 6 x 10(4) for mouse reticulocytes. In addition a competitive binding assay was used to estimate, relative to mouse plasma as a standard, the amounts of transferrin in supernatants separated from the first-stage cell suspensions. These measurements indicated that the transferrin contents per g tissue were approx 550 ug for tumor, approx 300 ug for spleen and thymus. (Author abstract) (8 Refs)

## 22. STUDIES ON THE UPTAKE OF 67GA AND 59FE AND THE BINDING OF TRANSFERRIN BY CULTURED MOUSE TUMOUR CELLS.

**Sephton RG, Harris AW**

**Cancer Inst, 481 Little Lonsdale St., Melbourne 3000, Australia**

**Int J Nucl Med Biol; 8(4):333-339 1981**

Two cultured mouse tumor cell lines, HPC-108 (myeloma) and WEHI-22 (T lymphoma), were used in an investigation of transferrin promotion of 67Ga and 59Fe uptake by malignant cells. The effectiveness of added human transferrin could be readily demonstrated on the cells in culture medium containing fetal calf serum, but transferrin-promoted uptake varied considerably between different batches of the serum. In serum-free medium, transferrin at concentrations as low as 1 ug ml-1 promoted substantial uptake of 67Ga and maximal uptake of 59Fe. Saturation of the transferrin with iron pre-empted its activity toward both tracers, indicating their transport requires binding to the same sites on transferrin. High affinity receptors for transferrin on the tumor cells were characterized by measurement of the binding of diferric 125I-labeled human transferrin to whole cells at 15 C. The HPC-108 line possessed 4 x 10(5) receptor per cell, WEHI-22 1.5 x 10(5) per cell, the EMT6 sarcoma line only 5 x 10(4) per cell, all with a dissociation constant of 1.4-2.3 nM. Some aspects of 67Ga and 59Fe uptake were explained by the characteristics of this receptor and the previously demonstrated difference between the two tracers in affinity for transferrin. (Author abstract) (16 Refs)

## 23. BIPHASIC UPTAKE OF IRON-TRANSFERRIN COMPLEX BY L1210 MURINE LEUKEMIA CELLS AND RAT RETICULOCYTES.

**Takahashi K, Tavassoli M**

**(c/o Tavassoli) Dept. Medicine, Veterans Admin. Hosp., Univ. Mississippi Sch. Medicine, Jackson, MS, 39216**

**Biochim Biophys Acta; 685(1):6-12 1982**

The kinetics of the cellular uptake of iron-transferrin complex was studied in L1210 murine leukemia cells and rat reticulocytes using 125I-transferrin. Saturation of transferrin with iron was necessary for optimal uptake. Following the incubation of cells with the radiolabeled complex a biphasic pattern of uptake was observed. The initial phase was rapid and relatively temperature-independent and was not altered by ethylamine, an inhibitor of transglutaminase activity which is necessary for receptor-mediated endocytosis. This phase was considered to result from receptor-ligand interaction which could be reversed to a great degree by replacement with unlabeled transferrin. A plateau was then reached, indicating a saturation of receptors. After 30 min a second phase of uptake was indicated by the second rise in the curve. This phase was slow, relatively temperature-dependent and could be abolished by ethylamine. It was interpreted as evidence of internalization of the ligand. Analysis of the data from competition studies with unlabeled transferrin indicated that the first phase might itself comprise a reversible and an irreversible step with a ratio of 5 to 1.4 for bound transferrin. Thus, the cellular uptake of iron-transferrin complex may consist of a reversible ligand-receptor interaction. Conformational changes may render this interaction irreversible and the internalization of the ligand may then follow. (Author abstract) (39 Refs)

## 24. IDIOTYPES: THEIR PRESENCE ON B- AND T-LYMPHOCYTES AND THEIR ROLE IN THE REGULATION OF THE IMMUNE RESPONSE.

Bankert RB, Bloor AG, Jou YH
Dept. Immunology Res., Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Vet Immunol Immunopathol; 3(1/2):147-184 1982

Experimental evidence consistent with the idea that idiotype (ID) recognition plays a vital role in the regulation of expression of individual clonotypes during an immune response is presented and discussed. Main sections include: idiotypes as markers on membranes of B- and T-lymphocytes, immunoregulatory mechanism based upon ID recognition, and future direction of research on the ID-anti-ID network of immune recognition. Although the understanding of cell mediated immunity in domestic animals is far from complete, it appears similar to that of man and experimental animals, with some differences. (398 Refs)

## 25. DIFFERENTIATION OF C3B RECEPTORS ON HUMAN LYMPHOCYTES, PHAGOCYTES, ERYTHROCYTES AND RENAL GLOMERULUS CELLS BY MONOCLONAL ANTIBODIES.

Dierich MP, Mussel HH, Scheiner O, Ehlen T, Burger R, Peters H, Schmitt M, Trepke S, Zimmer G
Inst. Medical Microbiology, Johannes Gutenberg-Univ., Angust-platz, D-6500 Mainz, W. Germany
Immunology; 45(1):85-96 1982

C3b receptor protein was purified from human erythrocytes by 2 M KBr solubilization and affinity chromatography on C3-coated sepharose. This material served as antigen for raising monoclonal antibodies. To investigate the distribution and antigenic relationship between the receptors for C3b on human erythrocytes, lymphoid and phagocytic cells, as well as kidney cells three monoclonal antibodies were selected which inhibited the binding of EAC14 23b to complement receptor-bearing cells. This could be shown for human erythrocytes by inhibiting the immune adherence reaction, for tonsil lymphocytes, Raji cells, and guinea-pig spleen cells by inhibition of rosette formation of these cells with EAC14 23b, and for human renal glomeruli by blocking of the adherence of EAC14 23b to kidney sections. In contrast, these monoclonal antibodies were not capable of inhibiting rosette formation of human granulocytes and monocytes with EAC14 23b. The antibodies only interfered with the rosette formation, of EAC14 23bi and EAC14 23d with Raji cells and tonsil lymphocytes - if at all - at high concentrations, whereas the rosette formation of Raji cells and tonsil lymphocytes with EAC14 23b was influenced by supernatants of the selected clones up to a dilution of 1:10(3) to 1:10(5). (Author abstract) (24 Refs)

## 26. MECHANISM OF ENHANCED COMPLEMENT-DEPENDENT CYTOTOXICITY OF PAPAIN-TREATED LYMPHOCYTES: EVIDENCE FOR INCREASED STABILITY OF CLASSICAL PATHWAY C3 CONVERTASE.

Lublin DM, Grumet FC
(c/o Grumet) Dept. Pathology, L-235, Stanford Univ. Sch. Medicine, Stanford, CA, 94305
J Immunol; 128(2):866-870 1982

The mechanisms of enhanced antibody-mediated, complement-dependent cytotoxicity caused by proteolytic treatment of cells was studied in a model system based on HLA microlymphocytotoxicity methods. In this model, papain treatment of lymphocytes resulted in (a) no change in antibody binding, (b) a slight decrease in initial binding of C4, (c) a marked increase in stability of cell-bound C4b, resulting in (d) an increase of cell-bound C3, and (e) no increase in lytic efficiency of the C5b-9 membrane attack complex. We conclude that the most important step in papain enhancement of lysis of lymphocytes is an increased stability of cell-bound C4b, possibly through decreased surface binding of C4-bp. This mechanism may be relevant to the pathologically increased lysis of cells occurring in patients with hereditary erythroblastic multinuclearity with a positive acidified-serum test (HEM-PAS). (Author abstract) (34 Refs)

## 27. FEEDBACK REGULATION OF IMMUNE RESPONSES BY IMMUNE COMPLEXES; POSSIBLE INVOLVEMENT OF A SUPPRESSIVE LYMPHOKINE BY FCRGAMMA-BEARING B CELL.

Miyama-Inaba M, Suzuki T, Paku YH, Masuda T
(c/o Masuda) Inst. Immunology Faculty Medicine, Kyoto Univ., Yoshida, Sakyo, Kyoto 606, Japan
J Immunol; 128(2):882-887 1982

Inoculations of antigen-antibody complexes (immune complexes) with the intact Fc portion generates suppressor cells in vivo by binding to FcRgamma on B cells via Fc portions. The cell type responsible for the suppression appears to be B cells bearing FcRgamma. Neither T cells nor macrophages participate in both the inductive and effective phases of this type of regulation. The suppression caused by splenic B cells, previously stimulated with immune complexes in vivo, is mediated by humoral factor(s) released from them. The suppressive factor(s) have H-2 gene product(s) coded by the right-hand side of the H-2 gene complex, but not for FcRgamma themselves or immunoglobulins. It has shared component(s) with suppressive B cell factor (SBF) released from FcRgamma+ B cells stimulated with immune complexes in vitro, and it resembles SBF in its mode of action. These findings indicate that immune complexes, the final products of antibody responses, control the immune responses by stimulating surface FcRgamma on B cells. It is of interest that this type of regulation functions in vivo. (Author abstract) (45 Refs)

## 28. DETERMINATION OF TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE ON BONE MARROW SMEARS BY IMMUNOPEROXIDASE.

Stass SA, Dean L, Peiper SC, Bollum FJ
Div. Pathology, St. Jude Children's Res. Hosp., 332 North Lauderdale, Memphis, TN, 38101
Am J Clin Pathol; 77(2):174-176 1982

Terminal deoxynucleotidyl transferase (TdT) is a marker of lymphoblastic disorders. Previously, the technique for determining TdT on smears was by indirect immunofluorescence. An immunoperoxidase procedure for detecting TdT on smears is reported. Results are in a comparable range with the indirect immunofluorescent technique. As discussed in this paper, TdT by immunoperoxidase may offer certain advantages over the indirect immunofluorescent procedure. (Author abstract) (8 Refs)

### 29. BLOOD LYMPHOCYTE SUBPOPULATIONS IN MYCOSIS FUNGOIDES AND THEIR FUNCTIONS IN VITRO.

Gu SQ, Petrini B, Von Stedingk LV, Thyresson N, Wasserman J
Dept. Dermatology, Karolinska Sjukhuset, S-104 01 Stockholm 60, Sweden
Acta Derm Venereol (Stockh); 61(6):487-490 1981

T-lymphocyte subpopulations, PWM stimulated in vitro Ig production by mononuclear cells, and spontaneous cell-mediated cytotoxicity (SCMC) were determined in patients with Mycosis fungoides (MF) as well as in sex- and age-matched normal controls. We were able to confirm our earlier findings of a significantly higher frequency of T-lymphocytes with Fc-receptors for IgG (Tg cells) and a proportion of T lymphocytes with Fc receptors for IgM (Tm cells) not significantly differing from normal controls. As defined by monoclonal antibodies, the proportion of T-helper cells (Leu3A) was significantly lower, whereas the T-suppressor cells (Leu2A) were in the range of normal controls. The PWM stimulated and spontaneous Ig synthesis in vitro was lower in MF patients whereas there was no difference in the SCMC activity, in comparison with normal controls. The lower frequency of T-helper cells in the peripheral blood may be explained by their migration to the skin. (Author abstract) (14 Refs)

### 30. T LYMPHOCYTES WITH FC-IGG RECEPTORS IN SKIN CANCERS.

Vena GA, Angelini G, D'Ovidio R, Lospalluti M, Meneghini CL
Dept. Dermatology, Univ. Bari, Bari, Italy
Acta Derm Venereol (Stockh); 61(6):555-558 1981

The proportion of peripheral blood lymphocytes with receptors for the Fc fragment of IgG (Tg) has been investigated in 25 patients with squamous cell carcinoma of the skin, in 25 patients with basal cell carcinoma of the skin, and in 33 controls. In patients with squamous cell carcinoma the results showed elevated values for Tg lymphocytes and a negative correlation between these T cells and the lymphocyte response to PHA and ConA. In patients with basal cell carcinoma the values for Tg lymphocytes were normal. (Author abstract) (12 Refs)

## LYMPHOCYTE AND DIFFERENTIATION ANTIGENS

### 31. MONOCLONAL ANTIBODIES THAT DETECT DIFFERENTIATION SURFACE ANTIGENS ON HUMAN MYEL OMONOCYTIC CELLS.

Perussia B, Trinchieri G, Lebman D, Jankiewicz J, Lange B, Rovera G
Wistar Inst., 36th St. at Spruce, Philadelphia, PA, 19104
Blood; 59(2):382-392 1982

We describe here the production and characterization of several new monoclonal antibodies that recognize differentiation antigens present on human cells of the myelomonocytic lineage. The lineage and the stage specificities of our reagents (myeloid-, monocytic-, and myelomonocytic-specific) were determined on the basis of their reactivity with human cell lines and with human peripheral blood and bone marrow cells. Cross-competition experiments demonstrated that some of the antibodies react with the same or closely associated antigenic determinants. Five antigens have been identified in this way: one present on myeloid, one on monocytic, and three on both myeloid and monocytic cells. The possible relationship of our antibodies with other established monoclonal antibodies is discussed, in addition to their use in the in vitro study of the differentiation pathways of human hemopoietic cells and in the characterization of leukemias. (Author abstract) (29 Refs)

### 32. MONOCLONAL ANTIBODIES TO HUMAN MACROPHAGE AND LEUCOCYTE COMMON ANTIGENS.

Becker GJ, Hancock WW, Kraft N, Lanyon HC, Atkins RC
(c/o Atkins) Dept. Nephrology, Prince Henry's Hosp., St. Kilda Road, Melbourne, Victoria 3004, Australia
Pathology; 13(4):669-680 1981

Three monoclonal antibodies have been made to identify cells of the human mononuclear phagocyte system in fluids and tissues. The first, PHM 1, recognizes a surface antigen common to all leukocytes. The other two antibodies, PHM 2 and PHM 3, bind to monocytes and macrophages but not to polymorphonuclear cells (PMN). PHM 2 labels all monocytes, macrophages and a small population of T-cells. PHM 3 labels most monocytes and macrophages but no other blood cells. The application of these monoclonal antibodies to the identification of mononuclear phagocytes in blood and liver using an unlabeled antibody immunoperoxidase (PAP) technique is demonstrated. (Author abstract) (32 Refs)

### 33. PHENOTYPE OF RAT NATURAL KILLER CELLS DEFINED BY MONOCLONAL ANTIBODIES MARKING RAT LYMPHOCYTE SUBSETS.

Cantrell DA, Robins RA, Brooks CG, Baldwin RW
Cancer Res. Campaign Lab., Univ. Nottingham, Nottingham NG7 2RD, England
Immunology; 45(1):97-103 1982

The fluorescence-activated cell sorter and a rosette-depletion technique were used to separate rat spleen lymphocytes and BCG-activated lymphocytes into subpopulations with and without the antigens defined by W3/13, W3/25 and OX8 monoclonal antibodies. The resultant populations were then tested for natural killer (NK) activity in a quantifiable 6 hr 51Cr release assay. The data establish that rat natural killer cells are heterogeneous with respect to their surface antigen expression and that subpopulations of rat NK cells express the OX8 and W3/13 defined antigens. However, rat NK cells do not express the antigen defined by W3/25 monoclonal antibody. (Author abstract) (20 Refs)

### 34. IN SITU IMMUNOLOGIC CHARACTERIZATION OF CELLULAR CONSTITUENTS IN LYMPH NODES AND SPLEENS INVOLVED BY HODGKIN'S DISEASE.

Poppema S, Bhan AK, Reinherz EL, Posner MR, Schlossman SF
(c/o Bhan) Dept. Pathology, Massachusetts General Hosp., Boston, MA, 02114
Blood; 59(2):226-232 1982

The cellular constituents in lymph nodes and spleens of patients with Hodgkin's disease were studied with a series of monoclonal antibodies directed against human thymocyte, peripheral T-cell, and Ia antigens. Utilizing both an immunoperoxidase technique on frozen tissue sections and indirect immunofluorescence on cell suspensions, we found that a majority of lymphocytes were T cells, since they stained with anti-T1 and anti-T3 antibodies, which react with all peripheral T cells. In addition, most of these cells were reactive with anti-T4 antibody, which defines the helper/inducer T-cell population,

whereas only a minority of cells stained with anti-T5 and anti-T8 antibodies, which are reactive with suppressor/cytotoxic T cells. Moreover, a large proportion of T cells expressed T10 antigen, which is found on activated T cells. A minority of the T cells also expressed Ia antigen(s), again suggesting that some of the T cells are activated. In contrast, the Reed-Sternberg cells did not react with any of these anti-T-cell antibodies or with anti-IgM antiserum, but displayed strong membrane and cytoplasmic staining with anti-Ia antibody. Taken together, these findings suggest that Reed-Sternberg cells are not of T-cell lineage but may be derived from antigen-presenting reticulum cells in the thymus-dependent areas of lymphoid tissues; these cells are normally associated with T4+ cells. (Author abstract) (40 Refs)

## 35. CELLULAR ORIGIN AND INTERACTIONS INVOLVED IN GAMMA-INTERFERON PRODUCTION INDUCED BY OKT3 MONOCLONAL ANTIBODY.

**Chang TW, Testa D, Kung PC, Perry L, Dreskin HJ, Goldstein G**
**Immunobiology Div., Ortho Pharmaceutical Corp., Raritan, NJ, 08869**
**J Immunol; 128(2):585-589 1982**

OKT3 monoclonal antibody, a human T cell mitogen, induced interferon production by cultured mononuclear cells at 10(-11) M concentrations. Interferon was secreted only under conditions wherein OKT3 was mitogenic, and production was correlated with cell proliferation. Thus, like mitogenesis, interferon secretion reached a peak 3 days after OKT3 stimulation, was inhibited by a factor(s) in human serum, and required 1,000x higher concentrations of Fab and F(ab')2 fragments of OKT3 for induction. The interferon was most likely of 'gamma' (immune) type, because pH 2 and 56 C treatments denatured it, whereas anti-alpha or -beta interferon antibodies did not. Mononuclear cells were fractionated into subpopulations that contained OKT4+ cells (helper/inducer T cells), OKT8+ cells (cytotoxic/suppressor T cells), and OKM1+ cells (monocytes) by combining sheep red blood cell rosetting and complement-mediated lysis using monoclonal antibodies against specific cell types. Both OKT4+ and OKT8+ cells proliferated upon OKT3 stimulation with the absolute requirement of OKM1+ cells. However, OKT4+ cells plus OKM1+ cells were necessary for the secretion of interferon. Studies with selective pretreatments with mitomycin C suggested that gamma-interferon was secreted by the OKT4+ cells and that the OKM1+ population subserved an accessory function. (Author abstract) (27 Refs)

## 36. A SUBSET OF HUMAN NATURAL KILLER CELLS ISOLATED AND CHARACTERIZED BY MONOCLONAL ANTIBODIES.

**Lohmeyer J, Rieber P, Feucht H, Johnson J, Hadam M, Riethmuller G**
**Medizinische Klinik, Klinikstrasse 36, D-6300 Giessen, W. Germany**
**Eur J Immunol; 11(12):997-1001 1981**

Monoclonal antibodies were induced against leukemic T cells from a patient with chronic lymphocytic leukemia exhibiting natural killer (NK) activity. Two antibodies, termed T811 and M522, reacted by indirect immunofluorescence with distinct subpopulations of normal human mononuclear blood cells. The antibody T811 defines a surface antigen which is restricted to a subset of the T cell lineage. The antigen recognized by the second antibody, M522, is expressed on monocytes and polymorphonuclear leukocytes and, in addition, on 9-17% of non-adherent peripheral blood leukocytes (NAL). It is shown that the total NK activity of NAL is confined to the subset of cells expressing the M522-defined antigen. Moreover, the portion of NK cytotoxicity associated with T lymphocytes is mediated by a subpopulation which is characterized by the simultaneous expression of the T811-and the M522-defined antigens. This population comprises about 4% of NAL and could be isolated to a purity of greater than 85%. (Author abstract) (20 Refs)

## 37. EXPRESSION OF T CELL DIFFERENTIATION ANTIGENS AND IA ON RAT CYTOTOXIC T LYMPHOCYTES.

**Duarte AJ, Carpenter CB, Strom TB**
**Lab. Immunogenetics and Transplantation, Brigham and Women's Hosp., Harvard Medical Sch., Boston, MA, 02115**
**J Immunol; 128(2):580-584 1982**

Study of lymphocyte subsets has been facilitated by the detection of various surface markers that are related to distinct functions. We have explored the use of affinity methods for separation of large quantities (10(8)) of rat cells and used this technique to identify surface markers of cytotoxic T lymphocytes. Splenocytes from animals bearing skin allografts for 7 days were depleted of B cells and were separated into T cell subsets by using W3/25 and OX8 monoclonal antibodies, which mark two nonoverlapping populations of peripheral T cells. Our results demonstrate that the cytotoxic T cells are W3/25-and OX8+. They also bear minimal or no Ag-F alloantigen, a peripheral T cell marker, and they express Ia-like products analogous to those of the mouse I-A subregion but not of the I-E/C subregion. (Author abstract) (27 Refs)

## 38. B LYMPHOBLAST ANTIGEN (BB-1) EXPRESSED ON EPSTEIN-BARR VIRUS-ACTIVATED B CELL BLASTS, B LYMPHOBLASTOID CELL LINES, AND BURKITT'S LYMPHOMAS.

**Yokochi T, Holly RD, Clark EA**
**(c/o Clark) Regional Primate Res. Center and Dept. Genetics, Univ. Washington, Seattle, WA, 98195**
**J Immunol; 128(2):823-827 1982**

Two new cell surface antigens expressed on B lymphoblastoid cell lines (B-LCL) were defined with cytotoxic mouse monoclonal antibodies. One marker, BB-1 (for B lymphoblast antigen-1), was detected on human and nonhuman primate B-LCL, Epstein-Barr virus (EBV)-activated B cell blasts, most Burkitt's lymphomas, and Ia+ B lymphoblast-like myelomas. Polyclonal B cell activators such as pokeweed mitogen (PWM) and lipopolysaccharide (LPS) also induced the expression of BB-1 on immunoglobulin (Ig)-positive cells.In contrast, BB-1 could not be detected on normal lymphoid tissues by complement-dependent cytotoxicity and immunofluorescence (IF) assays or by analysis with a fluorescence-activated cell sorter (FACS). T cell blasts, T cell leukemias, and pre-B cell or erythroblastic leukemia cell lines were also BB-1 negative. Of particular interest was the finding that BB-1 was expressed on the Jijoye lymphoma but only marginally on a subline of Jijoye, P3HR-1, that lacks receptors for EBV and produces a defective virus incapable of transforming lymphocytes. A second lymphoblast antigen (LB-1) unlike BB-1, was present on both T and B cell blasts and virus-transformed T- and B-LCL but not on normal lymphoid tissues. (Author abstract) (50 Refs)

## 39. BONE MARROW TRANSPLANTATION ACROSS MAJOR HISTOCOMPATIBILITY BARRIERS IN MICE. III. TREATMENT OF DONOR GRAFTS WITH MONOCLONAL ANTIBODIES DIRECTED AGAINST LYT DETERMINANTS.

Vallera DA, Soderling CC, Kersey JH
Dept. Therapeutic Radiology, Box 367, Mayo Memorial Building, 420 Delaware St., Southeast, Minneapolis, MN, 55455
J Immunol; 128(2):871-875 1982

We studied the effect of eliminating T cells from donor grafts of mice in a system in which bone marrow was transplanted across major histocompatibility barriers. BALB/c bone marrow (added as a source of hematopoietic stem cells) combined with equal volumes of spleen cells (added as a source of GVHD-promoting cells) was pretreated in vitro with monoclonal anti-Lyt-1.2 or Lyt-2.2 plus absorbed rabbit complement before injection into C57BL/6 total-body-irradiated recipients. Functional activity of anti-Lyt monoclonal antibodies was determined in CML assay. Treatment with anti Lyt-1.2 plus C did not have any ant i-stem cell activity, as measured by CFU-S assay, and protected recipients from the onset of lethal GVHD. Treatment with Lyt-2.2 plus C also did not reduce CFU-S; however, mice receiving treated marrow did develop GVHD and were all dead by 2 mo, as were untreated control mice. Surviving 'anti-Lyt-1.2 + C chimeras' demonstrated a high percentage of donor mononuclear cells in their peripheral blood. Similar results were obtained when C3H/HeN donor BMS was treated with monoclonal anti-Lyt-1.1 plus C and injected into C57BL/6 recipients. These findings show that monoclonal antibodies directed against determinants unrelated to Thy-1 can eliminate T cells in the presence of C and successfully protect transplanted mice from lethal GVHD. They also suggest that these anti-Lyt antibodies may be useful tools in determining subpopulations of T cells that contribute to the development of GVHD. (Author abstract) (24 Refs)

## 40. CELLS MEDIATING GRAFT REJECTION IN THE MOUSE. II. THE LY PHENOTYPES OF CELLS PRODUCING TUMOR ALLOGRAFT REJECTION.

Loveland BE, McKenzie IF
Dept. Pathology, Univ. Melbourne, Parkville, Victoria, 3052, Australia
Transplantation; 33(2):174-180 1982

The particular T cell subsets involved in the rejection of tumor allografts were examined in mice using two different approaches. In the first, EL4 lymphoma cells or B16 melanoma cells were given to ATXBM-CBA/H mice which had been reconstituted with either naive or sensitized T cells selectively depleted with either Ly-1 or Ly-2 monoclonal antibodies. In mice receiving nonsensitized T cells, Ly-123 cells and to a lesser extent Ly-1 cells were involved in the rejection of both tumors; Ly-23 cells played no role in this rejection. By contrast, in mice receiving sensitized cells, rejection was mediated by Ly-1 cells and not by Ly-123 or Ly-23 cells. In a second approach, sensitized cells were mixed with the tumor cells prior to injection into mice (the Winn neutralization assay). In this case, Ly-123 cells were the prime mediators of graft rejection. We conclude that both Ly-1 and Ly-123 cells can act as mediators of graft rejection. Ly-1-sensitized cells probably act as in a delayed-type hypersensitivity (DTH) response where few lymphocytes can lead to the rejection of many cells. In addition, Ly-123 cells can act as killer T cells but large numbers and the close apposition with the target cells are required. Our results also demonstrate a requirement for Ly-123 precursor cells in nonsensitized mice, probably acting as precursors for both types of effector cell. (Author abstract) (14 Refs)

## 41. GENETIC CONTROL OF SENSITIVITY TO MOLONEY LEUKEMIA VIRUS IN MICE: V. ROLE OF H-2-LINKED GENES IN THE CONTROL OF ANTI-FMR CYTOLYTIC T-LYMPHOCYTES.

Duprez V, Debre P, Levy JP
Laboratoire Immunologie et Virologie des Tumeurs, INSERM U 152, Hopital Cochin, Paris 14e, France
Cell Immunol; 65(2):317-324 1981

Three H-2-linked genes, Rmv1, Rmv2, and Rmv3 control the resistance of mice against Moloney virus (MLV)-induced leukemias. It has been shown previously that they function as immune response (Ir) genes regulating the level of antivirus antibodies. In the present experiments, the cell-mediated antitumor response has been studied in a series of inbred strains selected for their resistance or sensitivity to the MLV-induced disease. We failed to detect any relationship between resistance and sensitivity and the ability to produce cytolytic T lymphocytes (CTL) directed against the virus-induced FMR cell surface antigen. Furthermore, the role of each Rmv gene has been studied separately using congenic pairs of mice differing at only one of these loci: we failed to evidence any influence of these genes in the cell-mediated antitumor reactions as measured by the ability to lyse syngeneic FMR(+) target cells. Nevertheless a gene mapping in the D region of the MHC but probably different from RMv3 controls the response of a subset of anti-FMR CTL restricted by the H-2Kk antigens, with higher response in H-2Dd animals than in H-2Db animals. This observation confirms the existence of H-2D region associated Ir genes regulating the CTL-mediated antitumor immune responses by choosing the subset of responder CTL, and suggests that a fourth H-2-linked gene plays some role in the genetic control of the anti-FMR immune response. (Author abstract) (15 Refs)

## 42. RECOGNITION OF GIX-LINKED MINOR HISTOCOMPATIBILITY ANTIGENS BY H-2-RESTRICTED CYTOTOXIC T LYMPHOCYTES FROM C57BL/6-GIX+ MICE: AN APPROACH TO MAPPING THE GENES CONTROLLING GIX.

Green WR
Basic Immunology Program, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104
J Immunol; 128(2):920-925 1982

With the use of responder spleen cells from C57BL/6-GIX+ (B6-GIX+) congenic mice, in vivo priming with allogeneic AKR SL3 tumor cells and in vitro restimulation with E female G2 tumor cells lead to the production of cytotoxic effector cells that lysed both E female G2 and EL4 syngeneic target cells. This was in contrast to our previous findings with C57BL/6 (B6) mice that the same sensitization protocol resulted in the generation of CTL that vigorously lysed E female G2 and other H-2b-bearing tumors, which displayed the MuLV-associated Gross cell surface antigen (GCSA) but not GCSA-negative tumors such as EL4. Reciprocal competitive inhibition assays and H-2 restriction analyses indicated that two B6-GIX+ effector cell populations were generated: one, as with B6 CTL, recognized determinants unique to E female G2 and was Kb restricted, whereas the second recognized determinants common to E female G2 and EL4 and was Db restricted. This latter Db-restricted effector cell population could be exclusively raised b y restimulating AKR SL3-primed B6-GIX+ spleen cells in vitro with EL4 and could thus be characterized. Despite their broader specificity, these effector cells were found to be CTL, not NK cells. The AKR.H-2b SL1 tumor, all B6 tumors tested, and B6 spleen cells and thymocytes were

recognized by these CTL. Because neither B6-GIX+ nor 129 strain thymocytes or spleen cells were lysed, and because EL4 was GIX-negative, there was no correlation between GIX expression and target cell susceptibility. CTL of this specificity could also be generated by stimulating AKR SL3-primed B6-GIX+ responder cells in vitro with spleen cells from the following strains: AKR.H-2b, C57BL/10, B6, and B6/SKI, the subline from which the B6-GIX+ congenic was derived. These results suggested that the B6-GIX+ CTL of broad reactivity were directed against minor histocompatibility determinant(s) shared by the B6 and AKR strains but which differed in the B6-GIX+ and 129 strains. Furthermore, it appeared likely that this antigenic disparity arose as a consequence of the transfer of 129 strain genes closely linked to those controlling GIX expression during the process of deriving the B6-GIX+ congenic. These findings are discussed with respect to the utility of this system as an approach toward mapping the location of the GIX gene(s), and as a tool for the further genetic study of GIX. (Author abstract) (23 Refs)

### 43. INFORMATION TRANSFER BETWEEN THE MINOR ANTIGEN AND T CELL RECEPTOR REPERTOIRES.

Mitchison NA
Imperial Cancer Res. Fund Tumour Immunology Unit, Dept. Zoology, Univ. Coll. London, London, England
Scand J Immunol; 14(6):631-635 1981

Studies of information transfer between the minor antigen and T cell receptor repertoires are reviewed. T cells from A.TH x Balb mice were stimulated with irradiated cells from A.TL mice. T cell clones were tested for the capacity to help allogeneic or syngeneic B cells respond by reacting with surface determinants on target cells. A cell populations active in one system were also active in the other. Results indicate that a single major histocompatibility complex (MHC) determinant can stimulate allospecific proliferation and also serve as a receptor for allospecific helper activity. Studies with mouse strains bearing MHC recombinations showed that all clones reacted with AkalphaAkbeta (AkaAkb), the product of I-Ak. Some cells (Type II) reacted with AkaAkb regardless of other molecules on the stimulator cell. Other cells (TypeI) reacted more strongly to AkaAkb on A.TL cells than to AkaAkb on B10-type cells. Results suggest that lymphocytes react not to the MHC molecule alone, but to other molecules restricted by the MHC. Thus cells within an individual tolerate that individual's non-MHC molecules but can respond to the same molecules when they are restricted by foreign MHC molecules. Since non-MHC molecules are polymorphic, T cells vary in reactivi ty to cells bearing the same MHC but different non-MHC molecules. Non-MHC molecules thus control the allospecific antigen activity of the MHC, which in turn controls the repertoire of target cells to which T cells respond. (15 Refs)

## CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION

### 44. CONCOMITANT INDUCTION OF THE CELL SURFACE EXPRESSION OF IA DETERMINANTS AND ACCESSORY CELL FUNCTION BY A MURINE MACROPHAGE TUMOR CELL LINE.

Walker EB, Lanier LL, Warner NL
Immunology Lab., Univ. New Mexico Sch. Medicine, Albuquerque, NM, 87131
J Exp Med; 155(2):629-634 1982

The induction of cell surface Ia molecules on an Ia-negative, murine macrophage tumor, WEHI-3, and the subsequent ability of this Ia-induced tumor lines to provide accessory cell function in a major histocompatibility complex-restricted, antigen-driven, in vitro assay system are described. Uncharacterized soluble factor produced in concanavalin A-induced rat spleen cell suspensions had the capacity to induce the increased expression of cell surface H-2K and H-2D molecules and the expression of I-region gene products on murine monocyte-macrophage lineage tumors that were not Ia positive in the absence of the factor. (10 Refs)

### 45. SCANNING ELECTRON MICROSCOPIC STUDY OF CHANGES IN THE SURFACES OF LYMPHOKINE-TREATED GUINEA PIG MACROPHAGES.

Onozaki K, Homma Y, Miura K, Hashimoto T
Dept. Microbiology, Inst. Basic Medical Sciences, Univ. Tsukuba, Ibaraki-ken 305, Japan
J Reticuloendothel Soc; 30(6):471-481 1981

The surface architecture of guinea pig peritoneal exudate macrophages treated with partially purified lymphokines and cultured for different time periods was examined by scanning electron microscopy. Lymphokine-treated macrophages exhibited remarkable cell surface changes including enlarged petal-like ruffles as early as 2 hr after treatment. The characteristic ruffles were found in both rounded and spreading macrophages, indicating that the changes were common structural alterations of lymphokine-stimulated macrophages. However, macrophages in the control preparation or in the medium alone formed a few such enlarged ruffles. The formation of the unusual ruffles continued for 24 hr but disappeared after about 48 hr. Subsequently, the macrophages had numerous contracted cell surface ruffles with apparently smooth faces, and, after 72 hr, their surface architecture further changed to form more rough ruffles with acute angles. Because both macrophage migration inhibitory factor and macrophage activation factor were contained in the lymphokine preparation, the formation of such petal-like ruffles appeared to be related to the phenomena of migration inhibition and activation of macrophages. (Author abstract) (24 Refs)

### 46. LYMPHOKINES: THEIR ROLE IN LYMPHOCYTE RESPONSES. PROPERTIES OF INTERLEUKIN 1.

Oppenheim JJ, Stadler BM, Siraganian RP, Mage M, Mathieson B
Lab. Microbiology and Immunology, Natl. Inst. Dental Res., NCI, NIH, Bethesda, MD, 20205
Fed Proc; 41(2):257-262 1982

Interleukin 1, or IL 1, otherwise known as lymphocyte-activating factor, is a macrophage-derived 12,000-to 15,000-dalton polypeptide. Isoelectric focusing of human IL 1 reveals three

peaks at pI's of 5.2, 6.0, and 6.9, respectively. IL 1 can be depleted of lymphocyte-derived IL 2 by SP-Sephadex chromatography. IL 1 augments the mitogenic response of PNA- Lyt 1+ thymocytes, and promotes thymocyte helper functions and B cell antibody production. IL 1 induces stable E rosette formation and the production of lymphokines such as T cell growth factor (IL 2) by peripheral T lymphocytes. Others have shown that IL 1 or closely related factors also stimulate hypothalamic cells to induce fever; induce in vitro fibroblast growth, prostaglandin, and collagenase production; and stimulate hepatocytes to produce acute phase proteins such as serum amyloid A. Murine epidermal cells also produce a 15,000-dalton factor that is mitogenic for thymocytes and may be similar to IL 1. We have recently hybridized spleen cells from mice sensitized with partially purified human IL 1 with a myeloma cell line. Clones have been isolated that produce supernatants that partially inhibit the thymocyte proliferative response to IL 1 but not the T cell growth factor activity of IL 2. Should these hybridoma products prove to be monoclonal anti-IL 1 antibodies, they will facilitate the further purification and characterization of IL 1. (Author abstract) (43 Refs)

## 47. APPEARANCE OF THREE LYMPHOKINES IN CULTURE SUPERNATANTS HARVESTED AT DIFFERENT TIMES.

Yong WK, Halliday WJ
Dept. Microbiology, Univ. Queensland, St. Lucia, Qld. 4067, Australia
Immunol Lett; 4(1):21-26 1982

Factors responsible for WBC adherence inhibition (LAI), macrophage/WBC migration inhibition and acute erythrocyte-rosette augmentation (E-RA) were determined in culture supernatants of a fibrosarcoma induced in inbred CBA mice with 3-methylcholanthrene. Peritoneal cells from the mice were stimulated with the corresponding antigen and supernatants were prepared after incubation times of 1.0, 3.5, and 24 hr. Supernatants were tested by the indirect (two-stage) method on the same pool of indicator cells. The LAI inhibition factor was detected in both experiments in the 1 hr supernatant, in 1/2 at 3.5 hr, and not at all after 24 hr. The E-RA augmentation factor was found only in the 3.5 hr supernatant and the migration inhibition factor only in the 24 hr supernatant. Results indicate that the mediators responsible for the three in vitro reactions are different substances with different kinetics of production by stimulated cells. To assume only a single factor would involve consideration of a complex system o f distinct inhibitors. (25 Refs)

## 48. CELL SURFACE PHENOTYPE OF CYTOLYTIC T LYMPHOCYTE PRECURSORS IN AGED NUDE MICE.

Maryanski JL, MacDonald HR, Sordat B, Cerottini JC
Ludwig Inst. Cancer Res. (Brussels Branch), Ave. Hippocrate 74, UCL 74.59, 1200 Brussels, Belgium
Eur J Immunol; 11(12):968-972 1981

The cell surface phenotype of cytolytic T lymphocyte precursors (CTL-P) in congenitally athymic C57BL/6 nu/nu mice has been investigated. CTL-P were detected and quantitated in a limiting dilution mixed leukocyte microculture assay system supplemented with interleukin 2. Minimal estimates of the frequency of CTL-P among nylon wool passed (NWP) nude spleen cells were obtained following elimination of Thy-1-bearing or Lyt-2-bearing cells with monoclonal antibodies plus complement. Alternatively, NWP spleen cells bearing Thy-1 or Lyt-2 were positively selected on a cell sorter and assayed for CTL-P frequency. Both positive and negative selection techniques demonstrated that essentially all (greater than 98%) CTL-P in NWP nude spleen expressed Thy-1 and that the majority (80-90%) expressed Lyt-2. In control NWP spleen cells from normal C57BL/6 mice, greater than 98% of CTL-P were positive for both Thy-1 and Lyt-2. These data demonstrate that most functional alloreactive CTL-P developing in the apparent absence of thymic influence already express both Thy-1 and Lyt-2 prior to exposure to antigen. (Author abstract) (25 Refs)

## 49. INDUCTION OF FCRALPHA ON MURINE LYMPHOCYTES BY IGA IN VITRO.

Yodoi J, Adachi M, Masuda T
(c/o Masuda) Inst. Immunology, Faculty Medicine, Kyoto Univ., Yoshida, Sakyo, Kyoto 606, Japan
J Immunol; 128(2):888-894 1982

The regulatory influence of IgA on the expression of Fc receptors specific for IgA (FcRalpha) on mouse spleen cells was studied. In normal BALB/c spleen cells, the proportion of FcRalpha-bearing (FcRalpha+) cells was less than 2%, determined by the rosette formation with IgA-coated sheep red blood cells (SRBC) or with trinitrophenylated (TNP) SRBC after incubation with soluble MOPC 315 IgA, which specifically binds with TNP. There was no marked increase of FcRalpha+ cells after 24-hr culture in IgA-free medium or treatment with acid pH (pH 5.0). When cultured with MOPC 315 IgA for 18 hr, there was a dose-dependent increase of the cells binding TEPC 15 IgA-coated SRBC as well as the cells forming rosettes with TNP-SRBC. Twenty to 30% of spleen cells expressed FcRalpha when cultured with 300 ug/ml IgA. The induced receptors bound both soluble IgA and IgA-coated SRBC, and proved to be specific for IgA by the inhibition with other isotypes. The induction of FcRalpha by IgA was inhibited by the inhibitors of RNA and protein synthesis (actinomycin, puromycin, cycloheximide), and required more than 8 hr of culture for the expression. Mitom ycin (50 ug/ml) failed to inhibit the induction, indicating that proliferation of the cells is not required. FcRalpha was induced by dimer IgA but not by monomer IgA. Reduction of IgA with 0.02 M dithiothreitol resulted in the loss of inducing ability. However, reduced IgA competitively inhibited the induction of FcRalpha by nonreduced IgA and cytophilic binding of nonreduced IgA to the receptor. FcRalpha was induced by IgA on spleen cells depleted of adherent cells by Sephadex G-10 column passage. Both T and B lymphocytes were shown to express FcRalpha. (Author abstract) (34 Refs)

## 50. CHARACTERIZATION AND FUNCTIONAL PROPERTIES OF TUMOR CELL LINES IN ACCESSORY CELL REPLACEMENT ASSAYS.

Walker EB, Lanier LL, Warner NL
Immunobiology Lab., Dept. Pathology and Medicine, Univ. New Mexico Sch. Medicine, 2701 Frontier NE, Surge Building, Albuquerque, NM, 87131
J Immunol; 128(2):852-859 1982

This study reports the initial phenotypic and functional characterization of a series of cloned, murine, myelomonocytic tumors and their parent cell line WEHI-3, and a group of murine B lymphoma tumors. The tumor cell lines of the myelomonocytic lineage demonstrated the ability to reconstitute a macrophage-depleted, primary in vitro anti-SRBC PFC response, but only marginally enhanced an accessory cell-depleted, ova-primed, lymphocyte proliferation in vitro response. The B lymphoma tumors displayed exactly the reverse functional profile, being highly efficient in reconstitution of the proliferation response, but not supporting the SRBC PFC response. Detailed analysis of the cell surface phenotype of the

various B lymphoma tumors used in this study show they display cell surface markers characteristic of normal B lymphocytes but are heterogeneous in their various stages of differential arrest. Future work will concentrate on the orchestration of Ia-mediated and soluble factor-mediated (IL 1) modalities of antigen-triggering of lymphocytes by these B lymphoma and myelomonocytic tumor cell lines. (Author abstract) (46 Refs)

## 51. ACTIVATION OF RAT B LYMPHOCYTES. I. CHARACTERIZATION OF ANTI-IMMUNOGLOBULIN RESPONSES AND ISOTYPE DENSITY OF RAT B CELLS.

**Rosenberg JS, Feldman JD**
**Dept. Immunopathology, Scripps Clinic and Res. Foundation, La Jolla, CA, 92037**
**J Immunol; 128(2):651-655 1982**

Spleen cells of two rat strains, Lewis and Brown Norway (BN), have been activated by lectins and by antibodies specific for immunoglobulin isotypes embedded in their cell membranes. Optimal concentrations of antibodies specific for mu, gamma, or delta-chains of rat augments in vitro incorporation of 3H-TdR 5 to 18-fold in Lewis B lymphocytes and 1.5 to 4-fold in BN B lymphocytes. In addition, F(ab')2 fragments of anti-Ig reagents induced Lewis splenic B cells but not BN B cells to incorporate 3H-TdR. Responses to LPS and dextran sulfate, B lymphocyte mitogens, measured by radioactive uptake, were 5 to 10 times greater in Lewis B cell populations than in BN B cell populations. Density of surface Ig isotypes and capping kinetics were similar in the two rat strains, although the percentage of T cells, T cell subsets, B cells, and Ia+ B cells differed in the spleens of these strains of rats. Both T lymphocytes and macrophages were needed in culture to effect an optimal response. IL-2 restored the response in B cell cultures depleted of T cells and macrophages, and enhanced 3H-TdR uptake in whole spleen cells of Lewis but not BN rats. The strain-dependent responsiveness of B cells to specific anti-Ig reagents or B cell mitogens appears to be associated with inherent (genetic) defects in T cells and B cells or defects in T cell to B cell cooperation in BN rats. (Author abstract) (36 Refs)

## 52. MOUSE ERYTHROCYTE ROSETTE FORMATION. A MARKER FOR RESTING B LYMPHOCYTES.

**McGraw DJ, Kurec AS, Davey FR**
**(c/o Davey) Dept. Pathology, State Univ. New York Upstate Medical Center, 750 E. Adams St., Syracuse, NY, 13210**
**Am J Clin Pathol; 77(2):177-183 1982**

The ability of peripheral blood lymphocytes to form rosettes with mouse erythrocytes was examined using lymphocytes from normal healthy individuals of various ages and neoplastic lymphoid cells from patients with a variety of lymphoproliferative disorders. Our results indicated that only B lymphocytes form mouse rosettes (MR). The percentage of MR varied slightly according to the strain of mouse erythrocytes used in the assay. Little variation in the mean percentage of MR was observed when lymphocytes from various age groups of healthy individuals were studied. When neoplastic lymphoid cells were incubated with mouse erythrocytes only lymphocytes from patients with chronic lymphocytic leukemia formed an increased number of MR. Peripheral blood B lymphocytes lost their ability to form MR following incubation with pokeweed mitogen. These findings supported the view that the determinant on B lymphocytes which binds to mouse erythrocytes was present only at a resting stage of B cell maturation. (Author abstract) (36 Refs)

## 53. PRELIMINARY CHEMICAL AND BIOLOGIC CHARACTERIZATION OF (FC)TRF: AN FC FRAGMENT-INDUCED T CELL-REPLACING FACTOR.

**Thoman ML, Weigle WO**
**Dept. Immunopathology, Scripps Clinic and Res. Foundation, La Jolla, CA, 92037**
**J Immunol; 128(2):590-594 1982**

Fc fragment stimulation of Lyt-1+2-T lymphocytes triggers release of a T cell-replacing factor, here called (Fc)TRF. Chemical and biologic characterization of (Fc)TRF has been undertaken to provide information for its comparison with other T cell factors. Preliminary chemical characterization by column chromatography and isoelectric focusing suggest (Fc)TRF activity resides in a class of acidic molec ules that fall into two size classes of 58-60,000 daltons and 35-40,000 daltons. This factor is distinct from interleukin 2 (IL 2) as it has no T cell growth-promoting or costimulator activity, although it can also be generated by Con A activation of murine spleen cells. By these results (Fc)TRF has been defined as a unique T cell-replacing activity that promotes differentiation of B lymphocytes to antibody-secreting cells. (Author abstract) (25 Refs)

## 54. TNP-MODIFIED SYNGENEIC CELLS ENHANCE IMMUNOREGULATORY T CELL ACTIVITIES SIMILAR TO ALLOGENEIC EFFECTS.

**Eastman AY, Lawrence DA**
**Dept. Microbiology and Immunology, Albany Medical Coll., Union Univ., Albany, NY, 12208**
**J Immunol; 128(2):926-931 1982**

The ability of TNP-modified syngeneic B cells (TNP-B cells) to alter unprimed T cell regulation of in vitro humoral immune responses to sheep erythrocytes was examined. High doses of T cells (greater than 10(6)) suppressed TNP-B cell activation, and irradiation of the T cells (1000 R) abolished this suppression, revealing a significant degree of radioresistant help in the T cell preparations. Similarly, help was enhanced when the T cells were irradiated and co-cultured with semiallogeneic B cells (Allo-B cells). T cells (less than 10(6)) pretreated with mitomycin C provided a greater degree of help to both TNP-B cells and Allo-B cells than the untreated T cells; however, significant mitomycin C-resistant suppression was apparent with higher doses of T cells. In contrast to T cell regulation induced by TNP-B cells and Allo-B cells, help provided to unmodified syngeneic B cells was of lower magnitude and was relatively sensitive to irradiation and mitomycin C treatment, and suppressor activities were not as apparent. In 'bystander' and 'membrane-segregated' cultures TNP-modified B cells also augmented T cell activities with features similar to those stimulated by allogeneic cells: (i) Irradiated, TNP-modified stimulator cells induced a significant degree of bystander help that was radioresistant. Allo-B cells also enhanced bystander help, although significant bystander suppressive effects also were apparent with high T cell doses. (ii) The helper activity induced by TNP-B cells and Allo-B cells was mediated primarily by diffusible factors, and the production of the factors was radioresistant. (iii) The release kinetics of the helper factors were similar, in that optimal helper activity was observed by 48 hr. In contrast, factor-mediated help observed with unmodified syngeneic cells was minimal and attained optimal levels at 72 to 96 hr. In conclusion, TNP-modified syngeneic B cells stimulated T cell activities, leading to the enhancement of nonantigen-specific help and suppression with characteristics similar to positive and negative allogeneic effects, respectively. This study indicates that immunoregulatory T cell

function can be modulated by self-altering agents. (Author abstract) (40 Refs)

### 55. VARIANTS OF THE RAT BASOPHILIC LEUKEMIA CELL LINE FOR THE STUDY OF HISTAMINE RELEASE.

Siraganian RP, McGivney A, Barsumian EL, Crews FT, Hirata F, Axelrod J
Lab. Microbiology and Immunology, Natl. Inst. Dental Res., Bethesda, MD, 20205
Fed Proc; 41(1):30-34 1982

Cloning of the rat basophilic leukemia (RBL) cell lines demonstrates variability in cell chromosome number (approx 44-70) and in their capacity to release histamine following an IgE- or Ca++-ionophore stimulus. After IgE activation there is increased phospholipid methylation, Ca++ influx, arachidonic acid, and histamine release. On Ca++-ionophore A23187 stimulation, phospholipid methylation is not increased, but Ca++ influx, arachidonic acid, and histamine release occur. Variants of the RBL-cloned sublines defective at different stages in the release process were obtained and used to sequence the different events in the release process: IgE activation is followed by methylation, Ca++ influx, arachidonic acid, and histamine release. However, there are other variants with defects in intermediate steps in the pathway, eg, increased phospholipid methylation that is not followed by Ca++ influx or arachidonic acid release not followed by histamine release. Isolating variants carrying drug-resistance markers made hybridization (reconstitution) experiments possible. Two variants were recognized, each of which was deficient in one of the two phospholipid methyltransferase enzymes. Neither of these two variants released histamine; hybrids formed by fusion of these two cell lines have both phospholipid methyltransferase enzymes and release histamine. By other complementation experiments, groups of variants with defects at different steps in the histamine release sequence were recognized. Clearly, these basophilic leukemia cell lines provide a unique system for the study of the mechanism of histamine release. (Author abstract) (25 Refs)

### 56. SIALYLTRANSFERASE ACTIVITY AS A MARKER FOR THE DIFFERENTIATION OF LYMPHOCYTES. INCREASE IN SIALYLTRANSFERASE ACTIVITY OF BLASTS FROM ACUTE LYMPHOBLASTIC LEUKAEMIA CASES BY 12-O-TETRADECANOYLPHORBOL-13-ACETATE (TPA).

Sasaki R, Takaku F, Lin YL, Bollum FJ
Dept. Hematology, Jichi Medical Sch., 3311-1 Yakushiji Minamikawachi-Machi, Kawachi-Gun, Tochigi 329-04, Japan
Clin Exp Immunol; 47(2):381-388 1982

The level of sialyltransferase activity in leukemic blasts from acute lymphoblastic leukemia (ALL) cases was significantly lower (3.29 +-2.09 pmoles/5 x 10(7) cells or 1.77 +-1.16 pmoles/mg protein) than those (18.80 +-4.91 pmoles/5 x 10(7) cells or 7.72 +-1.75 pmoles/mg protein) of mature lymphocytes from normal volunteers (t less than 0.001). An inverse relationship between the level of sialyltransferase activity and the level of terminal transferase (TdT) activity was seen in blasts from eight TdT-positive A LL cases. No significant difference was observed in the level of sialyltransferase activity between ALL and cells of chronic myelogenous leukemia (CML) in blast crisis. Short term culture of ALL blast cells with 12-O-tetradecanoylphorbol-13-acetate (TPA) at the concentration of 10(-6) M to 10(-9) M caused a marked increase in sialyltransferase activity. In one of these three ALL cases the population of TdT-positive cells and the TdT activity of the blasts decreased significantly after culture with TPA. These results suggest that biochemical differentiation of leukemic lymphoblasts has been induced by the addition of TPA, although morphological changes were not observed. Sialyltransferase activity may be a useful indicator for the analysis of differentiation of lymphocytes. (Author abstract) (25 Refs)

### 57. HISTIOCYTIC DIFFERENTIATION OF MOUSE MALIGNANT FIBROUS HISTIOCYTOMA-LIKE TUMOR CELLS BY CULTURING WITH SODIUM BUTYRATE.

Tanaka H, Mori Y, Akedo H
Dept. Cell Biology, Center for Adult Diseases, Osaka 1-3-3, Nakamichi, Higashinari, Osaka 537, Japan
Cell Biol Int Rep; 6(1):85-90 1982

The histiocytic origin of the mouse malignant fibrous histiocytoma-like tumor was strongly suggested from butyrate-induction studies of cultured cells. Fc and C3 receptors and lysosomal enzyme activities were significantly induced in the two MFH cell lines studied 4 days after the addition of butyrate. The application of these results to the histogenesis of human malignant histiocytoma is briefly discussed. (10 Refs)

## EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS

### 58. INTERFERON-INDUCED CHANGES IN THE MONOCYTE MEMBRANE: INHIBITION BY RETINOL AND RETINOIC ACID.

Rhodes J, Stokes P
Immunology Div., Addenbrooke's Hosp., Hills Road, Cambridge, CB2 2QQ, England
Immunology; 45(3):531-536 1982

The effects of human interferon-beta on human peripheral blood monocyte function were examined in vitro. Interferon-beta was shown to increase substantially the expression of both Fcgamma receptors and HLA-DR antigens defined by monoclonal antibody. Retinol and retinoic acid were found to be antagonistic to these effects of interferon and physiological concentrations were sufficient to inhibit changes in the monocyte membrane induced by relatively high concentrations of interferon. (Author abstract) (31 Refs)

### 59. CHARACTERIZATION OF A NEW TYPE OF THYMOMA VARIANTS SUPERSENSITIVE TO DEXAMETHASONE.

Mermod JJ, Intriere L, MacLeod CL, Bourgeois S
(c/o Bourgeois) Regulatory Biology Lab., Salk Inst., P.O. Box 85800, San Diego, CA, 92138
J Steroid Biochem; 15:25-34 1981

Some of the properties of dexamethasone supersensitive (Dexss) clones derived from two murine T-cell lines, W7 and T1M1, are described. In the presence of 10(-7) M dexamethasone (Dex), bot h supersensitive variants are killed faster than their parental line, but the phenotype appears stable. Both Dexss variants have the same number of glucocorticoid receptor sites/cell: approx 37,000 Dex binding sites/cell in W7 line and its Dexss variants, and 31,000 sites in the T1M1 line and its Dexss variant. The affinity of these receptors for dexamethasone appears also unchanged in the Dexss variants. No significant difference in the rate of phosphorylation between the pa-

rental W7 line and the Dexss variant, and no significant effect of Dex treatment were noticed. Results of lactate and glycogen production studies indicate that no change along the pathway accounts for the supersensitive phenotype of the W7 Dexss variant, and that the pathways are not affected by glucocorticoids in these cells. The supersensitive variant Dexss W7 is more sensitive to cyclic (c)AMP than the parental line; they are approx 10x more sensitive than both T1M1 parental line and the Dexss variant to cAMP. In the presence of 10(-7) M Dex, the addition of calcium has no significant effect on the cell density reached after 24 hr either by the W7 line or its Dexss variant or by T1M1 line and its Dexss variant. General changes in membrane permeability do not account for the supersensitive phenotype of the W7 Dexss variant. (29 Refs)

## 60. MODULATION OF LEUKAEMIA BLAST COLONY GROWTH BY STEROID HORMONES.

**Taetle R, Guittard JP**
**Univ. Hosp. H720, 225 Dickinson St., San Diego, CA, 92103**
**Br J Haematol; 50(2):247-255 1982**

The effect of steroid hormones on in vitro colony growth of human myelogenous leukemia cells was examined. Beta-estradiol,testosterone and 5-beta-dihydrotestosterone had little effect on HL60 promyelocytic leukemia cells or blast colony forming cells (CFC) from eight patients with acute non-lymphocytic leukemia (ANLL). These compounds inhibited blast colony growth at very high concentrations (10(-6)-10(-4) M). In contrast, hydrocortisone (HC) had highly variable effects on blast colony growth. HL60 cells were resistant to HC at concentrations up to 10(-4) M but blast CFC showed a wide range of response. Some patients were resistant to HC at all concentrations tested, while others were inhibited by concentrations as low as 10(-8) M. The inhibitory effect of HC was also observed on 3H-TdR incorporation by stimulated peripheral blood blasts. Inhibition by HC was not blocked by progesterone, suggesting this effect was not mediated by specific hormone receptors. These data indicate differences in the response of blast cells in ANLL and normal progenitors to steroid hormones. Cells from patients with ANLL display variable inhibition by HC which is probably not mediated by specific receptors. (Author abstract) (30 Refs)

## 61. PATHOGENESIS OF TOXIC EFFECTS OF BERYLLIUM AND ITS COMPOUNDS.

**Alekseeva OG**
**Inst. Industrial Hygiene and Occupational Diseases, Moscow, USSR**
**Gig Tr Prof Zabol; (12):15-20 1981**

Pathogenesis of toxic effects of beryllium (BE) and its compounds is reviewed. Primary mechanisms of BE toxicity include damage of the cell membranes, phagocytosis of BE by macrophages, and activation of lymphocytes carrying BE receptors. Prolonged exposure to BE results in deficiency of suppressor function of immune system. Clinical manifestations of BE poisoning include pulmonary edema, development of lung granulomas, pulmonary and cardiovascular insufficiency, and myocardiodystrophy. The history of chronic berylliosis increases the risk of cancer development. (26 Refs) (In RUS)

## 62. THE ACTIVATION OF CLONED MACROPHAGES BY CONCANAVALIN A FOR TUMORICIDAL EFFECT: ASSESSMENT OF TUMOR CELL CYTOTOXICITY BY A CLONOGENIC ASSAY.

**Yen SE, Thomasson DL, Stewart CC**
**Div. Radiation Oncology, Malinckrodt Inst. Radiology, Washington Univ. Sch. Medicine, St. Louis, MO, 63110**
**J Cell Physiol; 110(1):1-8 1982**

Activation of the tumoricidal effect of mouse peritoneal exudate cell (PEC) macrophages by concanavalin A (Con A) is described, and data relating to possible mechanisms of the tumoricidal effect are analyzed. Macrophage cells activated by Con A (greater than or equal to 20 ug/ml) were rounded and hypertrophied, whereas unactivated cells or those treated with alpha-methyl-D-mannoside (AMM; 0.01 M), a specific receptor-binding inhibitor of Con A, retained the stretched shape with pseudopods characteristic of normal macrophages. Con A at concentrations greater than or equal to 20 ug/ml activated cloned macrophages for cytotoxicity against EMT-6 BALB/c mammary adenocarcinoma cells in a dose- and time-dependent manner. Macrophage survival (number of adherent cells) decreased as concentration of Con A increased, except when cells were coincubated with 0.01 M AMM. The activated state of PEC macrophages declined after Con A removal, but greater than or equal to 50% of the cytotoxic activity remained present up to 4 days. A cytoxic fluid released by PEC macrophages, direct tumoricidal effects of Con A, contamination of Con A, and Con A-binding effects are discussed as possible causes of the cytotoxic effect observed, but the exact mechanism remains unknown. (42 Refs)

## 63. EFFECT OF BM 12531 ON ROSETTE FORMATION AND IN VITRO FUNCTIONS OF PERIPHERAL BLOOD LYMPHOCYTES OBTAINED FROM HEALTHY DONORS AND CANCER PATIENTS.

**Advani SH, Ghogale SR, Gangal SG**
**Cancer Res. Inst. Tata Memorial Center, Parel, Bombay 400012, India**
**Indian J Med Res; 74:705-714 1981**

BM 12531 a 2-cynanaziridine derivative was tested for in vitro immunomodulation of peripheral blood lymphocytes from normal healthy donors, chronic myeloid leukemia patients in remission and untreated patients with Hodgkin's disease and multiple myeloma. The in vitro functions tested were active and total E rosette formation, PHA induced blastogenesis and production of PHA induced leukocyte migration inhibition factor. It was observed that incubation of lymphocytes with the drug at three concentrations (1.5 and 12.5 ug/ml) did not affect total or active E rosette formation significantly, while lymphocytes from 8/22 (36%) subjects showed increased uptake of 3H TdR in response to PHA in combination with the drug. There was no obvious dose dependency within the drug concentrations tested, although 5 ug/ml of the drug showed more potentiating activity. The drug was most active in induction of LMI factor by mitogen, especially in experiments where, initially the mitogen alone did not produce the lymphokine. BM 12531 did not seem to potentiate effectively, the T cell functions in malignancies characterized by general immunosuppression, such as Hodgkin's disease and multiple myeloma. (Author abstract) (21 Refs)

## OTHER RELATED STUDIES

### 64. RECENT DEVELOPMENTS IN THE IMMUNODIAGNOSIS OF CANCER.

Mavligit GM
Dept. Clinical Immunology and Biological Therapy, Univ. Texas M. D. Anderson Hosp. and Tumor Inst., Houston, TX
Cancer Bull; 33(6):250-254 1981

Recent developments in the use of carcinoembryonic antigen (CEA), beta-2-microglobulin, pancreatic carcinoma-associated antigens, prostatic carcinoma-associated markers, miscellaneous tumor-associated antigens, and monoclonal antibodies for immunodiagnosis of cancer are discussed. CEA is useful for early detection of recurrent disease following surgical resection of primary colorectal tumors. The possibility that unnecessary exploratory laparotomies are being performed as a result of more extensive use of serial CEA determinations is discussed; however, serial studies showing a persistent and progressive pattern of rising CEA justify an intensive effort toward tumor localization. Simultaneous determination of beta-2-microglobulin in cerebrospinal fluid and plasma indicates CNS involvement in patients with hematologic malignancies even earlier than the appearance of positive cytology and is used routinely in the total treatment plan of patients with acute leukemia and lymphoma. CEA levels in patients with pancreatic cancer are frequently higher than those in patients with disseminated colorectal cancer. New immunoassays based on pancreatic carcinoma-associated markers are being developed. Radioimmunoassay for prostate acid phosphatase is unlikely to be useful for prostatic carcinoma screening but may be used for more accurate staging. Other tumor-associated antigens include human chorionic gonadotropin, sialoglycoproteins, tissue polypeptide antigen, Tennessee antigen, beta-glucuronidase, and nucleolar antigens. Clinical trials are needed to show whether monoclonal antibodies have any advantage over conventionally prepared antisera in cancer immunodiagnosis. (21 Refs)

### 65. THE LATEST LABORATORY TESTS FOR CANCER.

Nichols WS, Nakamura RM
Dept. Pathology, Scripps Clinic and Res. Foundation, La Jolla, CA
Consultant; 21(6):131-134 1981

Screening procedures for cancer involving the use of tumor-associated antigens and endocrine-related, enzyme, virus-associated, and lymphocyte cell markers are described. The most useful tumor-associated antigens are those that have fetal components. Alpha-fetoprotein is an embryo-specific alpha-globulin that exists in healthy fetuses and in most persons with primary hepatic carcinoma. Elevated levels of carcinoembryonic antigen occur in many persons with colorectal cancer. Highest levels of pancreatic oncofetal antigen are found in patients with pancreatic carcinoma. Problems with specificity of tumor-associated antigens are discussed. Human chorionic gonadotropin assays are mainly used to monitor the progress of women who have been treated for hydatidiform mole or choriocarcinoma. An assay for pro-ACTH or ACTH may help distinguish between benign and malignant disease in patients with undiagnosed abnormalities that have been noted on x-ray films of the chest. A radioimmunoassay for calcitonin in the serum is useful in the diagnosis of medullary carcinoma of the thyroid. Plasma gastrin assay is a useful screening test for persons with severe peptic ulcer disease who are suspected of having Zollinger-Ellison syndrome. A thyroglobulin assay may be useful in the diagnosis of thyroid adenocarcinoma. Direct radioimmunoassay for serotonin in the serum or plasma is the test of choice for patients suspected of having carcinoid syndrome. 5-Hydroxyindoleacetic acid also may be used in the diagnosis of carcinoid syndromes. Estrogen receptor assays are useful in planning of therapy for breast cancer. (no Refs)

### 66. OT-CLL: A HUMAN T CELL CHRONIC LYMPHOCYTIC LEUKEMIA THAT PRODUCES IL 2 IN HIGH TITER.

Friedman SM, Thompson G, Halper JP, Knowles DM
Div. Rheumatology, Dept. Medicine, Columbia Univ. Coll. Physicians and Surgeons, New York, NY, 10032
J Immunol; 128(2):935-940 1982

This report identifies and describes a human T cell chronic lymphocytic leukemia, OT-CLL, which can be triggered by selected mitogens (either PHA or Con A) to produce IL 2 in high titer. Optimal IL 2 production requires culturing OT-CLL cells at 2 to 5 x 10(6)/ml for 24 hr in the presence of 1 to 2% PHA-M. Under these conditions, the titer of IL 2 generated is greater than 20-fold that obtained from conventional sources, eg, from mitogen-activated tonsillar lymphocytes. Two lines of experimental evidence suggest that the tumor cell product(s) is IL 2. First, in functional assays, supernatants derived from cultures of PHA-activated OT-CLL cells trigger the proliferation and long-term growth of IL 2-dependent human TCL cells. Second, a partial biochemical purification of the active moiety(ies) derived from OT-CLL demonstrates marked similarity to conventional human IL 2. Thus, the biologically active material(s) precipitates in 50 to 70% saturated (NH4)2SO4 solutions; elutes from DEAE-Sepharose in the presence of 0.04-0.08 M NaCl; and has an apparent mol wt of approx 14,000, as determined by Sephadex G-100 gel filtration. In addition, analysis of OT-CLL cells by indirect immunofluorescence, utilizing a panel of monoclonal antibodies, confirms not only that these tumor cells are of T cell lineage but that they display surface antigens that define the normal human peripheral T cell subset subserving helper or inducer function: OKT3+, OKT4+, OKT8-. (Author abstract) (36 Refs)

### 67. SEVEN MURINE CELL LINES WITH PROPERTIES OF MACROPHAGES.

Peters CJ
United States Army Medical Res. Inst. of Infectious Diseases, Fort Detrick, MD, 21701
J Reticuloendothel Soc; 30(6):453-470 1981

Seven phagocytic murine cell lines established from cultures of thymic lymphomas closely resembled authentic mouse peritoneal macrophages in their morphology and phagocytic properties. The cell lines secreted lysozyme and contained large quantities of nonspecific esterase, beta-glucuronidase, acid phosphatase, and lysozyme. The cell lines lacked the surface Ags of thymic lymphocytes (Thy-1.2 Ag) or bursa-equivalent lymphocytes (Ig), but they expressed receptors for Ig and complement. Complement-mediates rosettes did not occur in the absence of divalent cations. Efficient phagocytosis of sheep erythrocytes required opsonization with rabbit IgG Abs. Ia8 Ag was present on all four H2D cell lines. Two of the cell lines could be readily cloned, and we used these to demonstrate that variation in receptor expression and morphology was not due to the presence of multiple cell types. None of the cell lines was tumorigenic in nude mice or normal syngeneic mice. These macrophage-like cell lines provide well-characterized models which can be used to examine certain aspects of macrophage function under defined conditions without lymphoid cell admixture. (Author abstract) (37 Refs)

## 68. CELLULAR AND MOLECULAR PROPERTIES OF AN ANTIGEN-SPECIFIC CYTOTOXIC T LYMPHOCYTE LINE.

Bleackley RC, Havele C, Paetkau V
(c/o Paetkau) Dept. Biochemistry, Univ. Alberta, Edmonton, Alberta, T6G 2H7, Canada
J Immunol; 128(2):758-767 1982

Two cytotoxic T cell lines of CBA/J mouse origin have been generated, cloned, and characterized. One of these, MTL2, is cytotoxic for cells carrying the H-2(d) haplotype, the other MTL3, for H-2(b). Two clones of MTL2 differ significantly from each other in the morphology of the cells, although not in cytotoxicity. One has a higher number of intracellular vacuoles, or vesicles, and shows more of the typical attaching structures to the growth surface ('spikes') compared with the other. Cross-reactivity with a third-party alloantigen is enhanced by adding Con A to the cytotoxicity assay, but there is no self-killing either with or without Con A. The T cell lines show no rearrangement in their immunoglobulin heavy chain J and C(mu) genes. Normal T cells are also not rearranged, apparently, but normal B lymphocytes have both of their heavy chain alleles altered. Finally, cloned MTL2 cells contain less than five molecules of mu (IgM heavy chain constant region) mRNA per cell. (Author abstract) (39 Refs)

## 69. RAT NK CELLS ACTIVE AGAINST LYMPHOMA AND SARCOMA TUMOR CELLS ARE PROBABLY IDENTICAL.

Brooks CG, Flannery GR, Cantrell DA, Gray JD, Robins RA, Baldwin RW
Program Basic Immunology, Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
J Immunol; 128(2):913-919 1982

Rat NK cells, which lyse Mc7 sarcoma cells in a 6-hr chromium-release assay (CRA), have been shown previously to lack the characteristics of mature T cells, B cells, and macrophages, and to have low affinity Fc receptors but no C3 receptors. In these respects they are identical to those rat NK cells active against lymphoma cells. In this study we examined whether the rat NK cell-mediated lysis of sarcoma target cells and lymphoma target cells could be distinguished by additional methods, including those that have been claimed to distinguish these two effector systems in the mouse. Lysis of both types of target cell was studied in parallel by using a 4 to 6-hr CRA. The results showed that the two types of killer cells had similar age distribution and adherence to nylon wool, and preincubation in vitro caused augmentation of both activities. Normal spleen cells and BCG-activated peritoneal exudate cells (PEC) had equal proportions of anti-lymphoma and anti-sarcoma tumor NK activities, but evidence of a distinct subpopulation of anti-EL4 NK cells in activated PEC was found. Both killer cell types fractionated in the same manner on Percoll density gradients and were sensitive to anti-asialo GM1 serum and complement. Studies with the W3/13, W3/25, and OX8 monoclonal antibodies showed that rat NK cells were heterogeneous, but anti-sarcoma and anti-lymphoma killer cells had identical surface markers. Although lysis of some target cells occurred only after a pronounced lag period, this phenomenon was observed with both sarcoma and lymphoma targets. Sarcoma and lymphoma targets cross-competed in cold target competition assays. These results taken as a whole strongly suggest that in the rat, those NK cells that kill sarcoma cells and those that kill lymphoma cells, are identical. (Author abstract) (35 Refs)

## 70. HIGH-RESOLUTION ANALYSIS OF CHROMOSOME MARKERS IN BURKITT LYMPHOMA CELL LINES.

Zhang S, Zech L, Klein G
Dept. Medical Cell Genetics, Medical Nobel Inst. Karolinska Institutet, S-104 01 Stockholm, Sweden
Int J Cancer; 29(2):153-157 1982

Using a high-resolution chromosome banding technique, which provided more elongated and distinctly banded chromosomes, some new evidence was obtained for localization of break points in Burkitt lymphoma marker chromsomes. As a result, the characteristic translocation between chromosomes 8 and 14 was designated as t(8;14) (q24.1;q32.5) and the deletion of chromosome 15 was designated as del(15) (q13q15). (Author abstract) (19 Refs)

## 71. DIFFERENT T-CELL SUBTYPES ARE ASSOCIATED WITH PATHOLOGICALLY DISTINCT FORMS OF MOLONEY LEUKEMIA VIRUS (M-MULV)-INDUCED LYMPHOMA.

Aajo B, Skoog L, Fenyo EM, Klein G
Dept. Tumor Biology, Karolinska Institutet, S 104 01 Stockholm, Sweden
Int J Cancer; 29(2):163-167 1982

The T-cell enzyme markers, terminal deoxy-nucleotidyl transferase (TdT) and 20 alpha hydroxysteroid dehydrogenase (20 alpha SDH), were used to classify lymphomas induced by the Moloney leukemia virus (M-MuLV). Different subtypes of T cells were shown to be involved in different types of lymphoma. Thymomas were TdT-positive and grew as sc solid tumors at the site of inoculation. Spleen cells from mice with generalized lymphoma were of two types. In the majority of cases the lymphomas consisted of 20 alpha SDH-positive cells that homed to spleen and lymph nodes upon transplantation. In a few cases the cells of enlarged spleens were TdT-positive and, like the TdT-positive thymomas, could be transplanted as sc tumors. Thus, TdT-positive and 20 alpha SDH-positive T-cell lymphomas can be distinguished by their homing properties. Preleukemic thymus cells from M-MuLV inoculated mice can, after transfer to 400-R irradiated syngeneic hosts, induce new lymphomas by virus release or grow in an autonomous fashion in the recipients. Whether of donor or recipient type, these lymphomas are TdT-positive. In contrast, preleukemic bone marrow cells give lymphomas of donor type which are as heterogeneous for T-cell enzymes as are lymphomas induced by neonatal inoculation of M-MuLV. (Author abstract) (14 Refs)

## 72. DEFINITION OF A THY-1 DETERMINANT ON HUMAN NEUROBLASTOMA, GLIOMA, SARCOMA, AND TERATOMA CELLS WITH A MONOCLONAL ANTIBODY.

Seeger RC, Danon YL, Rayner SA, Hoover F
Dept. Pediatrics, Center Health Sciences, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA, 90024
J Immunol; 128(2):983-989 1982

Neuroblastoma, glioma, rhabdomyosarcoma, leiomyosarcoma, and teratoma cells were shown to express an antigenic determinant of human Thy-1 with monoclonal antibody 390 (ab 390). Specificity of ab 390 for a determinant on Thy-1 was shown in three ways. (1) The distribution of antigenic determinant 390 (ag 390) among normal cells and tissues was that of human Thy-1. Quantitative absorption of ab 390 with adult tissues demonstrated a large quantity of ag 390 associated with brain, at least 90-fold less associated with kidney, and 150 to 10,000-fold less associated with lung, thymus, liver, adrenal,

colon, and muscle. Ab 390 reacted strongly with cultured fibroblasts and also with 12% of thymocytes; it did not react with blood monocytes, lymphocytes, erythrocytes, or with bone marrow cells. (2) A molecule was isolated from deoxycholate solubilized human brain membranes by ab 390 affinity chromatography with Mr = 24,000. (3) Human brain Thy-1 that was purified by lentil lectin affinity chromatography specifically inhibited binding of ab 390 to LA-N-1 human neuroblastoma cells. In studies of 29 cultured tumor cell lines, ab 390 reacted strongly with gliomas and moderately with neuroblastomas, a rhabdomyosarcoma, a leiomyosarcoma, and teratomas. Its reactivity with medulloblastoma, melanoma, and carcinoma cell lines was weak or insignificant. A molecule with Mr = 26,000, which is the mw of fibroblast associated Thy-1, was purified from membranes of a neuroblastoma and a glioma cell line. Quantitative absorption of ab 390 with 50 noncultured tumors demonstrated that neuroblastomas, gliomas, and soft tissue sarcomas can express more ag 390 than all adult tissues except brain. Significant heterogeneity in the quantity of ag 390 associated with individual tumors within these positive classes was observed. These data suggest a variety of human tumor cells express Thy-1 on their surfaces. This expression appears to be appropriate for neuroblastoma, glioma, rhabdomyosarcoma, and leiomyosarcoma cells because normal cells of these same lineages also can express Thy-1. (Author abstract) (33 Refs)

## 73. TISSUE ORIGINS OF HUMAN POLYMERIC AND MONOMERIC IGA.

**Kutteh WH, Prince SJ, Mestecky J**
**(c/o Mestecky) Dept. Microbiology, Inst. Dental Res., Univ. Alabama Birmingham, Birmingham, AL, 35294**
**J Immunol; 128(2):990-995 1982**

Human tissues were examined for their ability to produce monomeric and polymeric forms of IgA in vitro. Mononuclear cells were examined for the presence of cytoplasmic immunoglobulins and J chain (by immunofluorescence) and for the amounts and molecular forms of intracellular and secreted IgA (by radioimmunoassay). Cultured bone marrow cells were the largest producers of total IgA, and approx 90% of the secreted IgA was monomeric. Spleen cells also produced predominantly monomeric IgA. Intestinal lamina propria cells secreted the greatest amounts of polymeric IgA, but also produced significant amounts of monomeric IgA. Tonsillar, lymph node, and peripheral blood cells produced approx equal proportions of monomeric and polymeric IgA. These results suggested that bone marrow may be a major source of serum monomeric IgA, and that lymphoid tissues associated with secretory surfaces may provide a greater proportion of polymeric IgA than other lymphoid tissues. There was a positive correlation between the production of polymeric IgA and the presence of cytoplasmic J chain; tissues that produced predominantly monomeric IgA generally displayed fewer cells containing cytoplasmic J chain. (Author abstract) (35 Refs)

## 74. GROWTH INHIBITION OF MALIGNANT HYPERNEPHROMA CELLS BY AUTOLOGOUS LYSOPHOSPHOLIPID INCUBATED MACROPHAGES OBTAINED BY A NEW METHOD.

**Berdel WE, Fink U, Egger B, Reichert A, Munder PG, Rastetter J**
**I. Medical Clinic, Technical Univ., Ismaningerstr. 22, 8000 Munich 80, W. Germany**
**Anticancer Res; 1(3):135-140 1981**

The in vitro inhibition of autologous hypernephroma cells by human macrophage after preincubation with alkyl-lysophospholipids (ALP) and a new method of purifying monocytes by adherence to teflon membranes are described. Fifty ml of peripheral blood was taken from four hypernephroma patients. After purification, the final cell yield was approx 50% of the monocyte count and the viability (trypan blue dye exclusion) of resuspended cells was greater than 98%. They showed all the morphological and cytochemical characteristics of human monocytes. After 5-10 days of cultivation the monocytes differentiated into monolayers of mature macrophages. Further incubation yielded epithelioid cells and multinucleated giant cells. Adult macrophages which were preincubated with different ALP inhibited the in vitro proliferation of autologous hypernephroma cells. The optimal concentration for both racemic-1-octadecyl-2-methyl-sn-glycero-3 phosphocholine and racemic-1-octadecyl-sn-glycero-3-phosphocholine was 1-5 ug/ml. Macrophages which were not incubated with these substances showed reduced inhibitory effects on the tumor growth. One of the four tested hypernephromas did not show a reproducible response to the antitumor effect of the macrophages. (20 Refs)

## 75. WARTHIN'S TUMOR: A FUNCTIONAL IMMUNOLOGIC STUDY OF THE LYMPHOID CELL COMPONENT.

**Howard DR, Bagley C, Batsakis JG**
**Dept. Pathology and Lab. Medicine, Maine Medical Center, Portland, ME, 04102**
**Am J Otolaryngol; 3(1):15-19 1982**

Immunologic functional studies, including B- and T-cell typing and mitogen stimulation, were conducted on lymphocytes of Warthin's tumor. Cells were obtained from two Warthin's tumors immediately after resection. The percentages of erythrocyte (E)-rosette-forming cells (T-cells) were 61% and 67% in the two tumors, respectively. Surface immunoglobulin was present in 34% of lymphoid cells in one tumor and in 6% in the other. The remaining cells did not mark as either T or B cells; the cells might represent non-marking cells (null cells). With 100 ug phytohemagglutinin (PHA), 82,800 disintegrations per min (dpm) were found in one case and 86,700 dpm in the other; the values were 81,500 and 223,800 dpm, respectively with 50 ug PHA, 1,600 and 185,400 dpm with 5 ug PHA, and 200 and 69,600 dpm with 1 ug PHA. Since the lymphocytes of Warthin's tumor manifest a proliferative activity in response to PHA, the validity of the immunologic marker studies in response to PHA and the validity of the immunologic marker studies defining the relative percentages of T and B cells are supported. The findings are discussed with respect to origin of the lymphoid component and histogenesis of Warthin's tumor. Morphologic findings and the immunologic studies support the concept that the lymphoid component of Warthin's tumor is derived from a pre-existing lymph node. (9 Refs)



* U. S. GOVERNMENT PRINTING OFFICE : 1982—361-847/121

# AUTHOR INDEX WITH CITATION NUMBERS


Abrahamsen AF 12
Adachi M 49
Advani SH 63
Akedo H 57
Alekseeva OG 61
Aman P 20
Angelini G 30
Asjo B 71
Atkins RC 32
Axelrod J 55
Bagley C 75
Baldwin RW 33
Baldwin RW 69
Bankert RB 24
Barsumian EL 55
Batsakis JG 75
Becker GJ 32
Bell R 9
Berdel WE 74
Berger R 11
Bernheim A 11
Bhan AK 34
Billing RJ 4
Bleackley RC 68
Bloom M 7
Bloor AG 24
Bollum FJ 28
Bollum FJ 56
Bourgeois S 59
Braun-Falco O 15
Brooks CG 33
Brooks CG 69
Burg G 15
Burger R 25
Bushkin Y 16
Cantrell DA 33
Cantrell DA 69
Carpenter CB 37
Catovsky D 1
Catovsky D 2
Cavo M 10
Cerottini JC 48
Cetto GL 13
Chang TW 35
Chilosi M 13
Clark EA 38
Crews FT 55
D'Ovidio R 30
Daniel MT 6
Danon YL 72
Davey FR 52
De Abrew S 21
De Giovanni C 10
Dean L 28
Debre P 41
Devaux C 17
Dierich MP 25
Dreskin HJ 35
Duarte AJ 37
Duprez V 41
Eastman AY 54
Egger B 74
Ehlen T 25
Fahey JL 4
Feldman JD 51
Fenyo EM 71
Feucht H 36
Fink U 74
Fiore-Donati L 13
Flannery GR 69
Foon KA 4
Ford RJ 14
Friedman SM 66
Galli MC 10
Gangal SG 63
Ghogale SR 63
Gobbi M 10
Godal T 12
Goldstein G 35
Gourdin MF 6
Gray JD 69
Green WR 42
Grilli S 10
Grumet FC 26
Gu SQ 29
Guglielmi P 6
Guittard JP 60
Hadam M 36
Hall K 20
Halliday WJ 47
Halper JP 66
Hammerling U 16
Han T 7
Hancock WW 32
Harmon JM 18
Harris AW 22
Hashimoto T 45
Havele C 68
Hirata F 55
Hoffmann-Fezer 15
Hoie J 12
Holly RD 38
Homma Y 45
Hoover F 72
Howard DR 75
Intriere L 59
Jankiewicz J 31
Janossy G 13
Janossy G 3
Jimenez Lopez A 5
Johnson J 36
Jou YH 24
Kersey JH 39
Kikutani H 16
Klein G 20
Klein G 70
Klein G 71
Knowles DM 66
Kraft N 32
Kung PC 35
Kurec AS 52
Kutteh WH 73
Landaas TO 12
Lange B 31
Langholm R 12
Lanier LL 44
Lanier LL 50
Lanyon HC 32
Lawrence DA 54
Lebman D 31
Lenoir G 11
Levy JP 41
Lillquist A 9
Lin YL 56
Lindmo T 12
Lohmeyer J 36
Lollini PL 10
Lospalluti M 30
Loveland BE 40
Lublin DM 26
Lundin G 20
MacDonald HR 48
MacLeod CL 59
Mage M 46
Marton PF 12
Maryanski JL 48
Masuda T 27
Masuda T 49
Mathieson B 46
Mavligit GM 64
McCaffrey R 9
McGivney A 55
McGraw DJ 52
McKenzie IF 40
Meneghini CL 30
Mermod JJ 59
Mestecky J 73
Minowada J 7
Mitchison NA 43
Miura K 45
Miyama-Inaba M 27
Mori Y 57
Munder PG 74
Mussel HH 25
Nakamura RM 65
Nanni P 10
Neal RM 19
Nichols WS 65
Nicoletti G 10
Nikolowski J 15
Niu EM 19
Onozaki K 45
Oppenheim JJ 46
Ozer H 7
Paetkau V 68
Paietta E 8
Paku YH 27
Peiper SC 28
Perry L 35
Perussia B 31
Peters CJ 67
Peters H 25
Petrini B 29
Pierce VK 19
Pierres M 17
Pizzolo G 13
Poppema S 34
Posner MR 34

Preud'Homme JL ..... 6
Preud'homme JL ..... 11
Prince SJ ..... 73
Prodi G ..... 10
Rastetter J ..... 74
Rayner SA ..... 72
Reichert A ..... 74
Reinherz EL ..... 34
Reyes F ..... 6
Rhodes J ..... 58
Rieber P ..... 36
Riethmuller G ..... 30
Robins RA ..... 33
Robins RA ..... 69
Rosenberg JS ..... 51
Rovera G ..... 31
Rubartelli A ..... 16
Sagawa K ..... 7
Sanchez Rodrigu ..... 5
Sasaki R ..... 56
Scheiner O ..... 25
Schlossman SF ..... 34
Schmidt TJ ..... 18
Schmitt M ..... 25
Schmoeckel C ..... 15
Schroff RW ..... 4
Schwarzmeier JD ..... 8
Seeger RC ..... 72
Sephton RG ..... 22
Sherman MR ..... 19
Siraganian RP ..... 46
Siraganian RP ..... 55
Sitia R ..... 16
Skoog L ..... 71
Soderling CC ..... 39
Sordat B ..... 48
Stadler BM ..... 46
Stass SA ..... 28
Stavnezer J ..... 16
Stewart CC ..... 62
Stokes P ..... 58
Strom TB ..... 37
Stunkel K ..... 15
Suzuki T ..... 27
Taetle R ..... 60
Takahashi K ..... 23
Takaku F ..... 56
Tanaka H ..... 57
Tavassoli M ..... 23
Testa D ..... 35
Thoman ML ..... 53
Thomasson DL ..... 62
Thompson EB ..... 18
Thompson G ..... 66
Thyresson N ..... 29
Trepke S ..... 25
Trinchieri G ..... 31
Tura S ..... 10
Vallera DA ..... 39
Vena GA ..... 30
Von Stedingk LV ..... 29
Walker EB ..... 44
Walker EB ..... 50
Warner NL ..... 44
Warner NL ..... 50
Wasserman J ..... 29
Weigle WO ..... 53
Yen SE ..... 62
Yodoi J ..... 49
Yokochi T ..... 38
Yong WK ..... 47
Zech L ..... 70
Zhang S ..... 70
Zimmer G ..... 25

# Compilation of Experimental Cancer Therapy Protocol Summaries

April 1982
Sixth Edition

COMPLIMENTARY COPIES
NOW AVAILABLE

## CONTENT

This document contains summaries of over 1200 open experimental clinical cancer therapy protocols from countries around the world.

Open protocols are arranged in sections according to the specific type of cancer.

Protocols closed in 1981 are listed by title, number, and investigator in a separate section.

## INDEXES

Tumor index
Agent/Modality index
Protocol identification number index

---

Mail to:
Compilation Request
ICRDB Program
National Cancer Institute
Westwood Building Room 10A18
Bethesda, Maryland 20205

Request for 1982 COMPILATION
(Print Clearly for use as mailing label)

Name: _____

Address: _____

_____

City/State/Zip: _____

Country: _____

# CANCER INFORMATION? CANCERLINE · CANCERLINE · CANCERLINE · CANCERLINE · CANCERLINE · CANCERLINE · CANCERLINE · CANCERLINE · CANCERLINE · CANCERLINE · CANCERLINE · CANCERLINE · CANCERLINE · CANCERLINE · CANCERLINE · CANCERLINE · JUST MENTION OUR NAME

**Mention CANCERLINE to your librarian** and the world's foremost collection of cancer information is at your disposal. With the help of this computerized data system, you can obtain information on the following:

## Cancer Literature

The literature date base, **CANCERLIT**, allows you to survey more than 3,000 biomedical journals for information on your topic of interest. Your search will also alert you to meeting proceedings, monographs, and books published in that area. Informative abstracts averaging 200 words are provided with each citation;

## Current Cancer Research

The data base **CANCERPROJ** allows you to retrieve descriptions of current work in any cancer research area. The descriptions, which state research objective, methodology, and experimental results, are supplied for projects underway in 77 countries around the world.

## Cancer Therapy Protocols

The **CLINPROT** section of CANCERLINE is designed primarily for clinicians. It provides detailed summaries of currently active experimental protocols for any cancer site, agent, or type.

**Ask your biomedical librarian about CANCERLINE.**

CANCERLINE is sponsored by the International Cancer Research Data Bank—a program of the National Cancer Institute.

CANCERLINE

# VIDEOTAPES

## ON CURRENT TOPICS IN CANCER RESEARCH

A pilot project of the International Cancer Research Data Bank (ICRDB) Program of the National Cancer Institute

*Three series are available . . .*

### THE RELATION OF CARCINOGEN ACTION ON DNA TO CELL TRANSFORMATION

| | | |
|---|---|---|
| PETER MAGEE<br>Fels Research Institute | *Keynote Address* | #VK01<br>28 min. |
| JAMES K. SELKIRK<br>Oak Ridge National Laboratories | *Metabolic Activation and Macromolecular Binding of Chemical Carcinogens* | #VK02<br>51 min. |
| PHILIP C. HANAWALT<br>Stanford University | *Cellular Responses to Damaged DNA* | #VK03<br>54 min. |
| CHARLES HEIDELBERGER<br>University of Southern California | *Mutagenesis and Oncogenic Transformation of Mouse Embryo Cells* | #VK04<br>54 min. |
| FRED RAPP<br>Milton S. Hershey Medical Center | *The Interaction of Herpesviruses and Host Cells Leading to Latency or Transformation* | #VK05<br>52 min. |
| | *Panel Discussion* | #VK06<br>31 min. |

### MECHANISMS OF METASTASIS

| | | |
|---|---|---|
| ISAIAH FIDLER<br>Frederick Cancer Research Center | *The Heterogeneous Nature of Cancer Metastasis and Implications for Therapy* | #VB01<br>47 min. |
| GEORGE POSTE<br>Smith, Kline and French Laboratories | *Phenotypic Analysis of Metastatic Cell Populations* | #VB02<br>42 min. |
| LANCE LIOTTA<br>National Cancer Institute | *Tumor Cell Invasion of Basement Membranes and Extracellular Matrices* | #VB03<br>33 min. |
| EVERETT SUGARBAKER<br>Miami Cancer Institute | *Some Clinical Characteristics of Metastasis in Man* | #VB04<br>41 min. |

### AUTOMATED CYTOLOGY

| | |
|---|---|
| Part One: Principles and Techniques | #VB05<br>56 min. |
| Part Two: Biological Applications | #VB06<br>52 min. |

VIDEOTAPES ON CURRENT TOPICS IN CANCER RESEARCH are in the 3/4" U-matic format and can be played on video equipment which accepts the NTSC standard (the standard for videotapes produced in the U.S.). The two Automated Cytology tapes (#VB05 and #VB06) are also available in the PAL format.

The videotapes are available on a loan basis. If you would like to schedule viewing for your group, or for more information, please write to:

Videotape Coordinator
ICRDB Program
Westwood Building, Room 10A18
Bethesda, MD 20205

Please specify three choices for viewing dates, and the tapes desired.

**U.S. DEPARTMENT OF COMMERCE**
**National Technical Information Service**
5285 Port Royal Road
Springfield, Va. 22161

OFFICIAL BUSINESS

Penalty for Private Use, $300

**PRINTED MATTER**

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF COMMERCE
COM-211

THIRD CLASS
BULK RATE

U.S.MAIL

CB-17

**CANCERGRAMS are distributed for the International Cancer Research Data Bank (ICRDB) by the National Technical Information Service (NTIS). CANCERGRAMS are available from NTIS on a standing order basis at $2 each for North American Continent addressees and $3 each for other addressees. An NTIS deposit account is required. For a list of subject categories or other information, please write to:**

**Subscription Section**
**National Technical Information Service**
**5285 Port Royal Road**
**Springfield, VA 22161**

**NOTICE OF MAILING CHANGE**

☐ Check here if you wish to discontinue receiving this publication.

☐ Check here if your address has changed and you wish to continue receiving this publication. (Be sure to furnish your complete address including zip code.)

Tear off cover with address label still affixed and send to:

Computer Support Center
ICRDB Program
IIT Research institute
10 West 35th Street
Chicago IL. 60616

CB17/82/08

NCI/ICRDB/CB17 82/08

PB82-931808

# ICRDB CANCERGRAM

# IMMUNOBIOLOGY AND CANCER

## Identification and Characterization of Immune Cells

SERIES CB17 No. 82/08

AUGUST, 1982

This Cancergram is a service of the INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM of the U.S. National Cancer Institute. Every few weeks, an updated Cancergram containing abstracts of selected cancer-related articles recently published in more than 3000 journals, and dealing with the topic indicated by the above title, is sent to researchers working in this area. These researchers are identified on the basis of the description of their current research project that has been submitted to the ICRDB Program, directly or via granting agencies.

This Cancergram is prepared by the Cancer Information Dissemination and Analysis Center (CIDAC) for Virology, Immunology, and Biology. ***If this Cancergram is useful and valuable, please send your comments to the CIDAC address below, since future editions depend on user satisfaction and user needs:***

CIDAC FOR VIROLOGY, IMMUNOLOGY, AND BIOLOGY
SCIENCE INFORMATION SERVICES
FRANKLIN INSTITUTE RESEARCH LABORATORIES
20TH AND RACE STREETS
PHILADELPHIA, PA 19103

NEWARK PUBLIC LIBRARY

SEP 13 1982

U. S. GOVT. PUBS.
DEPOSITORY 376

VISIT THE ICRDB EXHIBIT AT THE INTERNATIONAL CANCER CONGRESS IN SEATTLE, SEPTEMBER 8-15; MEET THE ICRDB STAFF, FIND OUT WHAT'S NEW, AND GET A FREE CANCERLINE SEARCH ON THE SPOT.

*In this issue:*


- CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS..... 1-16
- DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS..... 17-26
- LYMPHOCYTE AND DIFFERENTIATION ANTIGENS..... 27-44
- CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION..... 45-57
- EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS..... 58-67
- OTHER RELATED STUDIES..... 68-88


U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service • National Institutes of Health • National Cancer Institute

HE20.3173/2:

## CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS

### 1. CELL SURFACE MARKERS IN THE CHARACTERIZATION OF LEUKEMIAS.

Blackstock R, Humphrey GB
Dept. Pediatrics, Univ. Oklahoma Health Sciences Center, Oklahoma City, OK, 73190
Methods Cancer Res; 19:3-51 1982

Immunological markers of acute lymphoblastic leukemia (ALL) are reviewed. Methods used to identify receptors or antigens on lymphoid cells and lymphoblasts freshly isolated from human subjectes are emphasized. Rosette studies discussed include E-rosettes, rosettes with mouse erythrocytes, human au tologous rosettes, and rosettes with other erythrocytes. Surface and cytoplasmic immunoglobulin, Fc receptors, complement receptors, lymphocyte differentiation antigens, glucocorticoid receptors, peanut agglutinin receptors, and histamine receptors are also discussed. Recent clinical application of immunological markers of ALL only is reviewed with reference to heterogeneity, special variants and relapse ALL, and prognostic significance, although the principles described apply equally well to the use of immunological markers with the myeloid leukemias, the chronic leukemias, and immunodeficiency diseases. Immunological markers required for diagnostic evaluation of ALL are suggested. (421 Refs)

### 2. SURFACE MARKERS ON LEUKEMIC BLASTS AND THEIR PROGNOSTIC SIGNIFICANCE.

Sen L, Estevez ME, Finiasz MR, Giuntoli J, Pavlovsky S, Sackmann-Muriel F, Divito J, Dibar E
Departamento de Microbiologia, Instituto de Investigaciones, Hematologicas. Buenos Aires, Academia Nacional de Medicina, Argentina
Medicina (B Aires); 41(Suppl):109-117 1981

A retrospective analysis of surface markers (SM) on bone marrow lymphoblasts from 148 patients (1 mo to 39 yr old) with untreated acute lymphoblastic leukemia (ALL) is reported; tests were on cells obtained by bone marrow aspiration at the time of initial diagnosis. Determination of SM included testing for receptors for sheep erythrocytes at 4 C (E4) and 37 C (E37), complement (C3), mouse erythrocytes (ME), and surface immunoglobulins (sIg). Seventy-one percent of the patients had no SM studied. Of the remaining 43 patients, 24 showed only one SM and 19 had two or more: the patients were subdivided into four different groups. T-ALL included E4 or E37 and/or C3, B-ALL included C3 and sIg, C3-All had only C3, and ME-ALL had only ME. T-ALL was predominant in boys greater than 5 yr old with high WBC, while C3-ALL prevailed in girls with WBC less than 50,000/cubic mm. Patients without markers were evenly divided between the sexes; 56% were 5 yr old or less, and WBC was 50,000/cubic mm or less. The relationship between SM and response to treatment, aggressivity, duration of remission, clinical features, and prognosis are analyzed. (45 Refs)

### 3. GLUCOCORTICOID RECEPTORS IN LEUKEMIC CELLS OF CHILDREN WITH ACUTE LEUKEMIA.

Ido M
Dept. Pediatrics, Mie Univ. Sch. Medicine, Tsu, Japan
Mie Med J; 31(1):109-125 1981

Levels of glucocorticoid receptors (GCR) in leukemic cells in children with acute leukemia were measured. Blood samples were obtained from 80 patients (41 males and 39 females, 2 mo-22 yr old). Cases included 65 of acute lymphoblastic leukemia (ALL) and 15 of acute myeloblastic leukemia (AML). Binding of [3H]dexamethasone (DMS) was measured with whole cells and with cytosol fractions. Nuclear binding accounted for 60%, cytosol binding for 40%, of total binding. Nuclear binding was proportional to cytosol b inding and did not become saturated at DMS levels sufficient to saturate cytosol binding. With DMS levels sufficient to saturate GCR, equilibrium was approached after 90 min. GCR levels, in sites/cell, were 2,827-90,300 (mean 30,039) for patients with ALL and 2,348-40,936 (mean 14,207) for patients with AML. Normal lymphocytes had 1,926-11,438 (mean 6,620) sites/cell. Among patients with ALL GCR levels for 13 patients showing good response to glucocorticoid therapy were 15,050-90,300 (mean 45,451, median 32,508); for 7 patients relapsing within 1 yr 7,525-58,996 (mean 28,233, median 24,682); for 14 poor responders 2,227-22,876 (mean 7,765, median 4,816). Differences between good responders and poor responder were significant; differences between good responders and early relapsers were not significant. GRC levels can apparently be used to predict, to some extent, response to glucocorticoid therapy in patients with ALL, but not to predict duration of remission. (30 Refs)

### 4. PURINE AND PYRIMIDINE RIBONUCLEOSIDE MONOPHOSPHATE PATTERNS OF PERIPHERAL BLOOD AND BONE MARROW CELLS IN HUMAN ACUTE LEUKEMIAS.

Scavennec J, Maraninchi D, Gastaut JA, Carcassonne Y, Cailla HL
Case 906, Centre d'Immunologie INSERM-CNRS de Marseille-Luminy, 13288 Marseille Cedex 9, France
Cancer Res; 42(4):1326-1330 1982

Purine and pyrimidine ribonucleoside monophosphate (NMP) levels were measured in blood and/or bone marrow cells of groups of patients with acute leukemia including acute lymphoblastic leukemia (ALL) and acute nonlymphoblastic leukemia (ANLL). Patients were either untreated or in remission. Three relapsed patients with ALL were also studied. Phytohemagglutinin-stimulated tonsil lymphocytes and bone marrow cells both from normal subjects were used as controls. Moreover, observations in acute leukemias were compared with those in chronic leukemias. The cytidine, adenosine, guanosine, and uridine 2'-, 3'-, and 5'-monophosphate contents were measured by high-performance liquid chromatography. 2'- and 3'-NMP concentrations were 2.5x higher in ALL and were 5.5x higher in ANLL leukemic cells than in chronic leukemic blood cells or control bone marrow cells. 2'-NMPs were found only in leukemic blast cells and accounted for about 30% of 2'- and 3'-NMP mixtures. Levels of 2'- and 3'-NMP were around two- and four-fold higher in bone marrow than in peripheral blood cells of patients. The high level of 2'- and 3'-NMP found in bone marrow and blood cells of untreated ALL patients decreased during remission without reverting to normal; however, in relapse, it was 5 to 10x higher than in the case of untreated patients. The 5'-NMP concentrations were always lower than those of 2'- and 3'-NMP and were the same in acute leukemias and controls. Furthermore, 5'-NMP levels remained constant during the course of the disease. 2'- and 3'-NMP levels appear therefore to be u seful markers of leukemic blasts and may facilitate both the diagnosis of acute leukemia and the monitoring of chemotherapy. (24 Refs)

## 5. PHENOTYPE CHARACTERIZATION OF CHRONIC LYMPHOCYTIC LEUKEMIA WITH MONOCLONAL ANTIBODIES AND SURFACE RECEPTORS.

Estevez ME, Sen L, Diez RA, Bellonard A, Santos I
Departamento de Microbiologia, Instituto de Investigaciones, Hematologicas Academia Nacional de Medicina, Buenos Aires, Argentina
Medicina (B Aires); 41(Suppl):123-130 1981

Different immunologic and enzymatic techniques as well as monoclonal antibodies (MA) were used in 33 patients (21 men, 12 women; 42-84 yr old) with chronic lymphocytic leukemia. Analyses were performed when WBC was greater than 10,000/mm square. T cell markers were determined with sheep red blood cell rosette test (E4 and E37). B cell markers were determined using mouse red blood cell rosette formation test (ER). C3 serum complement was determined by erythrocyte antibody complement (EAC) rosette test. Cell surface (sIg) and cytoplasmic (cIg) immunoglobulins were determined by immunofluorescence. Surface antigens T1, T3, T4, T6, T8, T9, T10, T11a, Ia1, and M1 were evaluated with MA of OK series. All the patients had phenotype B and were divided into four groups (early immature, immature, mature, and very mature). EAC was present in all the patients, and only 1/3 had ER values greater than 20%. Range of values was 0-37% for E4, 0-27% for E37, 22-94% for EAC, and 0-82% for ER. Results of monoclonal antibodies were positive in 11/12 patients for Ia1, in 7/12 for T1, and in 2/12 for T10, all the others were negative. (16 Refs) (In SPA)

## 6. T-CHRONIC LYMPHOCYTIC LEUKAEMIA PRESENTING AS PRIMARY HYPOGAMMAGLOBULINAEMIA - EVIDENCE OF A PROLIFERATION OF T-SUPPRESSOR CELLS.

Thien SL, Catovsky D, Oscier D, Goldman JM, Van Der Reijden HJ, Melief CJ, Rumke HC, Ten Berge RJ, Von Dem Borne AE
(c/o Catovsky) MRC Leukemia Unit, Royal Postgraduate Medical Sch., Hammersmith Hosp., Ducane Road, London W12 0HS, England
Clin Exp Immunol; 47(3):670-676 1982

A 63-yr-old man with late onset hypogammaglobulinemia is described. Splenectomy, carried out because of marked splenomegaly and pancytopenia, demonstrated marked T lymphocytic infiltration in the splenic red pulp with prominent germinal centers. A persistent peripheral blood and bone marrow lymphocytosis ensued (10 x 10(9)/l and 40% respectively) and this was consistent with T-chronic lymphocytic leukemia (T-CLL). Over 88% of his blood lymphocytes were E+, OKT3+, OKT8+ and OKT11+; 54% of the T lymphocytes had receptors for IgG (Tgamma cells). Functional studies showed that the T lymphocytes of this parent lacked killer and natural killer cell function but they effectively suppressed the differentiation of normal B cells in a PWM stimulated system. It is suggested that the T-CLL in this patient resulted from the proliferation of the T suppressor subset which was responsible for his hypogammaglobulinemia. (Author abstract) (21 Refs)

## 7. 2' AND 3' RIBONUCLEOSIDE MONOPHOSPHATE IN LEUKOCYTES OF ACUTE MYELOID LEUKEMIA: MARKERS FOR EARLY DIAGNOSIS OF RELAPSE.

Scavennec J, Cailla H, Gastaut JA, Maraninchi D, Carcassonne Y
Centre d'Immunologie INSERM-CNRS de Marseille-Luminy, Case 906, 13288 Marseille Cedex 9, France
Int J Cancer; 29(3):257-259 1982

Levels of 2' and 3' purine and pyrimidine ribonucleoside monophosphates (2'-, 3'-NMP) in leukocytes from blood and/or bone marrow were measured in three adult patients with acute non-lymphoblastic leukemias. The measurements of 2'-, 3'-NMP were made by high-performance liquid chromatography (HPLC) at various times in the course of the disease. Complete remission (CR) was obtained for all three patients but two of these have since died after relapsing at 8 and 9 mo, respectively. The third patient remains in CR at 1.5 yr. The levels of 2'-, 3'-NMP in the leukocytes of the patient remaining in remission have not changed since the beginning of his remission. However, in the patients who relapsed 2'- and 3'-NMP levels increased first in bone marrow then in blood leukocytes. These increases occurred about 3 mo before the relapse was detected by morphological criteria. These data suggest that 2'-, 3'-NMP measurements may have a prognostic value if used to monitor patients with acute myeloid leukemia in CR. (Author abstract) (16 Refs)

## 8. HIGH AND LOW FC IGG-RECEPTOR EXPRESSION IN HUMAN CHRONIC GRANULOCYTIC LEUKAEMIA CELLS.

Harlozinska A, Potomski J, Lawinska B, Noworolska A, Richter R
Dept. Pathological Anatomy, Sch. Medicine, ul. Marcinkowskiego 1, 50-368 Wroclaw, Poland
Br J Cancer; 45(2):194-200 1982

Discontinuous density-gradient centrifugation was used to separate chronic granulocytic leukemia (CGL) cells in the chronic phase and blast crisis (BC) into fractions containing granulocytes in individual stages of maturation. The occurrence of the Fc IgG (FcR) and complement-component receptors (CR1 and CR2) in each fraction was estimated. It was established that, with increasing yields of mature granulocytes, the proportion of cells bearing Fc and C3 receptors increased. The most important finding was that the high- and low-receptor categories of CGL cells in chronic phase depended on the percentage of FcR+ cells. In the high-receptor CGL group, in addition to FcR, the proportion of CR1+ and CR2+ cells was also greater than in the low-receptor CGL group. Some differences in clinical course of both immunological CGL groups were observed. (Author abstract) (12 Refs)

## 9. IMMUNOLOGICAL CHARACTERIZATION OF NON-HODGKIN'S LYMPHOMA: ENRICHMENT OF NEOPLASTIC CELLS FROM LYMPHOID TISSUES AND BLOOD.

Bom-Van Noorloos AA, Van Beek AA, Ubels-Postma J, Zeijlemaker WP, Van Heerde P, Von Dem Borne AE, Cleton FJ, Melief CJ
(c/o Melief), Central Lab. Netherlands Red Cross Blood Transfusion Service, P. O. Box 9190, 1006 AD Amsterdam, The Netherlands
Cancer; 49(8):1605-1612 1982

Cell suspensions prepared from lymph nodes, spleen or peripheral blood of patients with non-Hodgkin's lymphoma (NHL) often contain a high percentage of residual nonmalignant cellular elements. By E-rosette sedimentation, it was possible to enrich such suspensions from patients with various types of lymphoma for malignant cells. In patients with a B- or non-B/non-T-cell lymphoma, the neoplastic cells were found in the non-T fraction. The capacity to respond to stimulation by various stimuli was then confined to the T-cell fraction, which contained the residual normal T-cells. In patients with T-cell lymphomas, in which the malignant cells had retained the capacity to form E-rosettes, lymphoma cells were found in the T fraction. These cells usually did not respond to mitogenic stimuli. Using this separation method, small proportions of neoplastic cells could be identified in mixed cell populations. Thus, in the blood from 9 out of 23 lymphoma patients without abnor-

malities in routine blood tests, a population of abnormal cells was detected after cell separation. This included a monoclonal B-cell population in the blood of four patients, a questionably monoclonal B-cell population in the blood of two patients and an increased non-B/non-T cell population in the blood of three patients. (Author abstract) (35 Refs)

## 10. NON-T, NON-B LYMPHOMAS ARE RARE IN CHILDHOOD AND ASSOCIATED WITH CUTANEOUS TUMOR.

**Bernard A, Murphy SB, Melvin S, Bowman WP, Caillaud J, Lemerle J, Boumsell L**

**Laboratoire d'Immunologie des Tumeurs de l'Enfant, Institut Gustave-Roussy, 94800 Villejuif, France**

**Blood; 59(3):549-554 1982**

Tumor cells from a total of 116 children with non-Hodgkin's lymphoma were studied for their pattern of reactivity with a battery of cell markers, including their capacity for spontaneous formation of sheep erythrocyte rosettes (E-rosettes), demonstration of surface immunoglobulins (SIg), and positivity with antisera against T-cell antigens, the common acute-lymphoblastic-leukemia-associated antigen (cALLa), and Ia-like antigens. Fifty-eight children (50%) had T-cell lymphomas, including all those with mediastinal tumors. Fifty children (43%) had B-cell lymphomas, including 44 of the 45 with abdominal primaries. Eight children (7%) non-T, non-B tumors, four of whom presented at a young age with cutaneous lymphoblastic tumors. These results demonstrate that the great majority of children with NHL, not leukemic at diagnosis, have tumors clearly committed to either T- or B-cell differentiation pathways and only rarely exhibit the common ALL phenotype (cALLa+, Ia+, E-, T-, SIg-), contrasting with the distribution of childhood lymphoblastic leukemias. The unusual association of these non-T, non-B cases with skin involvement has not previously been reported, raising speculation regarding patterns of lymphocyte traffic and origins of childhood lymphomas and leukemias. (Author abstract) (32 Refs)

## 11. CLINICAL AND HISTOPATHOLOGICAL STUDY OF NASAL T CELL LYMPHOMA.

**Yamanaka N**

**Dept. Otolaryngology, Sapporo Medical Coll., Sapporo, Japan**

**Jibi Inkoka; 53(12):1075-1086 1981**

Clinical and histopathological features of two cases with nasal T cell lymphoma in which an initial clinical diagnosis of 'rhinitis gangrenosa progressiva' or lethal midline granuloma was made. The histopathological examinations of their autopsy specimens proved that their nasological disease could all be identified to be malignant lymphoma arising from the nasal cavity, which showed, in general, histopathological characteristics described for T cell lymphoma derived from peripheral T cells. This histopathological observation was then confirmed by immunofluorescence studies using various antisera directing to either human T or B cell surface antigens, which clearly demonstrated that their malignant cells bore human T cell antigens but lacked human Ia-like antigens as well as surface immunoglobulins, indicating their peripheral T cell origin. These data may suggest that so-called 'rhintis gangrenosa progressiva' or lethal midline granuloma contains at least two distinct disease categories, one of which is Wegener's granulomatosis, and another of which is nasal T cell lymphoma described herein. (Author abstract) (25 Refs) (In JPN)

## 12. ADULT T-CELL LYMPHOMA-LEUKEMIA IN BLACKS FROM THE WEST INDIES.

**Catovsky D, Rose M, Goolden AW, White JM, Bourikas G, Brownell AI, Blattner WA, Greaves MF, Galton DA, McCluskey DR, Lampert I, Ireland R, Bridges JM, Gallo RC**

**Medical Res. Council Leukaemia Unit, Royal Postgraduate Medical Sch., London, England**

**Lancet; 1(8273):639-642 1982**

Six Black patients (5 born in the West Indies and 1 in Guyana), aged 21-55 yr, had adult T-cell lymphoma-leukemia diagnosed in the UK. This disorder is rare in Europe and the USA, but is more common in Japan. Five patients had severe hypercalcemia which correlated with disease activity, although osteolytic lesions were found in only one. Other clinical features were lymphadenopathy and a high white blood-cell count (range 27-67 x 10(9)/l) with a predominance of pleomorphic lymphoid cells with pronounced nuclear irregularities prominent at ultrastructural level. The cells in all cases formed rosettes with sheep red blood-cells and lacked terminal transferase. Analysis with OKT monoclonal antibodies in four cases confirmed a mature T-cell phenotype defined as helper/inducer (T4+, T6-, T8-) in three. Combination chemotherapy resulted in short-lived remissions; four patients died and two have survived 3-6 mo. The disease in these patients is indistinguishable on clinical and pathological grounds from adult T-cell leukemia/lymphoma in Japan. Geographical clustering among certain racial groups suggests common etiological factors in the pathogenesis of this disease. The finding of high titer antibody against the structural core protein (p24) of a new human C-type leukemia virus (human T-cell leukemia/lymphoma virus) in all tested cases from this series and data from all but one case from Japan suggest that one such factor may be viral. (Author abstract) (no Refs)

## 13. IMMUNOBLASTIC SARCOMA: MORPHOLOGIC CRITERIA AND THE DISTINCTION OF B AND T CELL TYPES.

**Maurer R, Taylor CR, Parker JW, Cramer A, Lukes RJ**

**Inst. Pathology, Univ. Hosp., CH-8091 Zurich, Switzerland**

**Oncology; 39(1):42-50 1982**

Immunologic concepts have facilitated the recognition within the histiocytic lymphoma group of the Rappaport classification of five diagnostic categories of lymphoma (follicular center cell lymphoma large cleaved and large non-cleaved types, immunoblastic sarcoma B cell type, immunoblastic sarcoma T cell type and 'true histiocytic lymphoma'). The first four of these 'large cell lymphomas' are closely related biologically and are difficult to distinguish histologically. This paper purports to examine the morphologic criteria employed in the differential diagnosis of these four large cell lymphomas in an objective manner, utilizing carefully prepared histologic sections from 24 cases of lymphoma that had been subjected to detailed B and T cell characterization by surface marker methods. Eighteen morphologic criteria were evaluated by four observers independently. The results show that reliable histologic distinctions can be made on histologic grounds in a proportion of cases only and that individual criteria show more overlap within diagnostic criteria than previously recognized. This is attributed in part to the close biologic relationship of these neoplasms. It is also recognized that the morphologic criteria are subtle and that the pathologist should have the advantage of auxiliary techniques - cytochemistry, immunohistology, surface marker techniques - to achieve reliable distinction of functional types within the diffuse histiocytic group of Rappaport. (Author abstract) (27 Refs)

## 14. IMMUNOHISTOLOGY OF GRAFT-VERSUS-HOST DISEASE MEDIATED SKIN LESIONS AND ITS CORRELATION TO A LARGE GRANULAR LYMPHOCYTE SURFACE PHENOTYPE AND FUNCTION.

Muller C, Schuch K, Pawelec G, Wilms K, Wernet P
Abteilung II, Medizinische Universitatsklinik Tubingen, Otfried-Muller-Strasse, D-7400 Tubingen, W. Germany
Blut; 44(2):89-94 1982

Skin biopsy specimens from five leukemia patients with graft-versus host disease (GVHD) were compared to specimens from normal individuals and from leukemia patients prior to treatment. Expression of cell-surface antigens was measured by immunofluorescence tests using selected monoclonal antibodies. Normal skin from two normal individuals and two leukemic patients showed human lymphocyte antigen (HLA)-ABC on all epidermal keratinocytes from the basal cell layer to the stratum granulosum and in the dermis on fibroblasts, mononuclear cells, blood vessel endothelium, and sweat gland epithelium. No HLA-ABC was found in the outer horny layer of epidermis. HLA-D/DR were found in the dermis on rare irregular mononuclear cells, a subpopulation of fibroblasts, and blood vessel epithelium. In the epidermis HLA-D/DR were found only on a small population of dendritic cells. Ia+, HLA-D/DR+ cells were concentrated in suprabasal epidermal layers. Skin from patients with acute GVHD showed normal distribution of HLA-ABC. Cells bearing HLA-D were concentrated in the upper dermis and at some points appeared to invade and destroy the basal cell layer of the epidermis. 1+, Ia+ Langerhans cells were reduced within the epidermis. Chronic GVHD was marked by hyperkeratosis in one case and general epidermal atrophy in one case. HLA-D+ mononuclear dermal cells and Langerhans cells were reduced in one chronic patient. Onset of chronic and acute GVHD was marked by infiltration of the dermis by HLA-D+ cells resembling mature T cells, suggesting that skin lesions result from cell-mediated cytotoxicity effected by a population of T cells. Skin biopsy may be useful as a diagnostic aid in GVHD. (9 Refs)

## 15. OCULAR ADNEXAL LYMPHOID NEOPLASMS: CLINICAL, HISTOPATHOLOGIC, ELECTRON MICROSCOPIC, AND IMMUNOLOGIC CHARACTERISTICS.

Knowles DM, Jakobiec FA
Lab. Surgical Pathology, Columbia Univ. Coll. Physicians and Surgeons, 630 W 168th St., New York, NY, 10032
Hum Pathol; 13(2):148-162 1982

Clinicopathologic analysis of 400 ocular adnexal lymphoid neoplasms has demonstrated that the orbital lymphoid neoplasms occur primarily in the 6th and 7th decades of life; that their benignancy or malignancy is generally indistinguishable clinically; that the orbital malignant lymphomas are most commonly small cell lymphomas; that the orbital 'histiocytic' lymphomas almost always represent an anomalous deposit of disseminated lymphoma; and that the percentage of patients with orbital lymphoma who develop systemic disease varies with the histopathology: two thirds of cases of poorly differentiated lymphocytic lymphomas, as defined cytomorphologically, have associated systemic disease. Prospective correlative clinicopathologic and immunologic analysis of 25 cases has shown that cell marker analysis divides the ocular adnexal lymphoid infiltrates into immunologically polyclonal proliferations, which show diverse but benign histopathologic features, and immunologically monoclonal B cell proliferations, which have the histologic features of malignant lymphomas. The benign, polyclonal ocular pseudolymphomas recapitulate the cell marker profile of a benign reactive lymph node with similar variations in the T cell:B cell ratio. The ocular adnexal and nodal B cell lymphomas are analogous in that they most commonly express surface IgM heavy chains and kappa light chains, express Ia antigens in parallel with SIg, and occasionally contain neoplastic B cells at various developmental stages - ie, Ia+SIg+ and Ia+SIg-. Correlative immunologic and ultrastructural studies have demonstrated that electron microscopy is a reliable and reproducible technique for indirectly assessing the mono- or polyclonality of an ocular adnexal lymphoid neoplasm. This study is focused on the use of hybridoma-derived monoclonal antibodies, which are capable of detecting maturational stages of B and T cell differentiation and functionally distinct T cell subsets, in order to investigate the interactional and immunoregulatory defects that participate in the generation of the ocular adnexal lymphoid proliferations. (Author abstract) (56 Refs)

## 16. STAGING, GROWTH PROPERTIES AND METASTATIC BEHAVIOR OF A TRANSPLANTABLE MURINE T-CELL LYMPHOMA.

Dullens HF, Hilgers J, Spit BJ, De Heer E, De Weger RA, Van Basten CD, Den Otter W
Dept. Pathology, State Univ. Utrecht, Pasteurstraat 2, 3511 HX Utrecht, The Netherlands
Int J Tissue React; 4(1):15-25 1982

The SL2 lymphoma, spontaneous tumor derived from the DBA/2 mouse, was characterized with respect to cell surface antigens, enzyme histochemistry, histology, tumor growth, and metastatic behavior. Cytotoxicity tests using rabbit antisera from thymic markers revealed that SL2 cells contain surface markers Th 1.2 and TL 1.2.3, indicating a T-cell origin for SL2. Immunofluorescence testing failed to reveal membrane immunoglobulins, a further indication that the cells are of the T-cell and not B-cell series. Histochemical staining of SL2 and DBA/2 derived thymocytes were positive for acid phosphatase, beta-glucuronidase, non-specific esterase, and alpha-naphthyl acetate esterase, and negative for ATPase and 5'-nucleotidase. The SL2 cells are well adapted to growth in vivo as well as in vitro. Survival studies of DBA/2 mice showed that an ip injection of 100 cells killed all the animals, while 1,000 cells were required for sc injection. The in vitro doubling time of SL2 cells was about 18 hr. SL2 cells injected either ip or sc metastasized first to extravascular positions in the liver and the capillaries of the alveolar septa of the lungs, and later to the kidney, spleen, heart and abdominal wall muscles, as revealed by light- and electron microscopy. Thus, the SL2 lymphoma has a T-cell phenotype, is highly malignant, growing both as an ascites or solid tumor, and exhibits metastatic behavior. The knowledge of the cell surface antigens may mak e this tumor line a useful model for immunotherapy investigations. (25 Refs)

## DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS

### 17. MONOCLONAL ANTIBODY TO TRANSFERRIN RECEPTOR BLOCKS TRANSFERRIN BINDING AND INHIBITS HUMAN TUMOR CELL GROWTH IN VITRO.

Trowbridge IS, Lopez F
Dept. Cancer Biology, Salk Inst. Biological Studies, P. O. Box 85800, San Diego, CA, 92138
Proc Natl Acad Sci USA; 79(4,part1):1175-1179 1982

A murine hybridoma has been obtained that produces a monoclonal antibody against the human transferrin receptor. In contrast to previously characterized monoclonal antibodies that recognize the transferrin receptor, this antibody, designated 42/6, blocks the binding of transferrin to its receptor and inhibits the growth of the human T leukemic cell line, CCRF-CEM, in vitro. Inhibition of cell growth was dose dependent, and as little as 2.5 ug of purified antibody per ml had a detectable effect, even though transferrin was present in the tissue culture medium in large molar excess. Cells grown in the presence of antibody for 7 days accumulated in S phase of the cell cycle. The addition of iron to antibody-treated cultures in the form of ferric complexes or ferrous sulfate did not overcome the growth inhibitory effects of the anti-transferrin-receptor antibodies. This result suggests that either transferrin is the only means by which CCRF-CEM leukemic cells can be provided with sufficient iron in vitro or that other factors in addition to iron starvation are involved in the antibody-mediated growth inhibition. The inhibition of cell growth by 42/6 monoclonal antibody suggests that monoclonal antibodies against proliferation-associated cell surface antigens, such as the transferrin receptor, may be useful pharmacological reagents to modify cell growth in vitro. (Author abstract) (46 Refs)

### 18. A MONOCLONAL ANTIBODY THAT DETECTS EXPRESSION OF TRANSFERRIN RECEPTOR IN HUMAN ERYTHROID PRECURSOR CELLS.

Lebman D, Trucco M, Bottero L, Lange B, Pessano S, Rovera G (c/o Rovera), Wistar Inst. Anatomy and Biology, 36th St. at Spruce, Philadelphia, PA, 19104
Blood; 59(3):671-678 1982

A monoclonal antibody, L5.1, obtained by immunizing a Balb/c mouse with HL60 human promyelocytic leukemia cells, was found to react with both HL60 cells and with the K562(S) cell line. This monoclonal antibody binds and immunoprecipitates a glycoprotein (Mr 87,000) present on the cell surface membrane of K562(S) as a disulfide bonded dimer. In competition experiments L5.1 competes with both transferrin and OKT9 (a known antitransferrin receptor antibody) for binding to target K562(S) erythroleukemia cells. Binding of both L5.1 and transferrin to the surface of K562(S) cells is inhibited by treatment with 12-O-tetradecanoyl-phorbol-13-acetate, and the extent and time course of inhibit ion is similar in both cases. Cell sorting analysis of normal human marrow cells incubated with L5.1 indicates that L5.1 reacts strongly with all the morphologically recognizable erythroid lineage precursors, from the pronormoblast to the orthochromatic normoblast, and with reticulocytes. Erythrocytes, myeloid elements, monocytes, megakaryocytes and platelets, peripheral blood B and T lymphocytes do not bind significantly with this antibody and only a small fraction of promyelocytes was reactive. Antibody L5.1 did not react with leukemic cells of patients with acute lymphoblastic, myeloblastic and promyelocytic leukemias, but it did react with some established B (1 of 5) and T (2 of 3) cell lines, and a myeloid (1 of 3) cell line, and with PHA-stimulated peripheral blood lymphocytes. The nonhemopoietic cell lines tested did not bind with L5.1 with the exception of a colorectal adenocarcinoma and a melanoma cell line, which were both strongly positive. The relationship of antibody L5.1 to other monoclonal antibodies that bind the transferrin receptor is discussed. (Author abstract) (35 Refs)

### 19. EPSTEIN-BARR VIRUS (EBV) RECEPTOR IMPLANTATION ONTO HUMAN B LYMPHOCYTES CHANGES IMMUNOGLOBULIN SECRETION PATTERNS INDUCED BY EBV INFECTION.

Tsukuda K, Volsky DJ, Shapiro IM, Klein G
Dept. Tumor Biology, Karolinska Institutet, S-104 01 Stockholm, Sweden
Eur J Immunol; 12(1):87-90 1982

Mosaic membrane vesicles containing both Epstein-Barr virus (EBV) receptors and Sendai virus envelope proteins were allowed to form by the previously described membrane solubilization and co-reconstitution technique. The vesicles were allowed to fuse with the membranes of normal human B lymphocytes, whereafter the cells were infected with transforming EBV (B95-8 substrain). Compared to similarly infected but otherwise unmanipulated cells, the receptor-implanted lymphocytes responded with a larger number of EBV-determined nuclear antigen positive and immunoglobulin-secreting plaque-forming cells (PFC). Moreover, there was a clear increase of the IgG/IgM PFC ratio in the receptor-implanted B lymphocytes. These results show that not all human B lymphocytes that can potentially be activated by EBV express functional EBV receptors. B lymphocytes programmed to secrete IgG appear to be more defective in this respect than IgM secretors. (Author abstract) (27 Refs)

### 20. LIGAND-INDUCED ASSOCIATION OF SURFACE IMMUNOGLOBULIN WITH THE DETERGENT-INSOLUBLE CYTOSKELETAL MATRIX OF THE B LYMPHOCYTE.

Braun J, Hochman PS, Unanue ER
Dept. Pathology, Harvard Medical Sch., Boston, MA, 02115
J Immunol; 128(3):1198-1204 1982

Ligand binding is believed to induce surface immunoglobulin (Ig) to form a physical association with the underlying cell cytoskeleton. We investigated this interaction by use of nonioni c detergents, which are known to dissolve membrane proteins but preserve a detergent-insoluble cytoskeletal residue. In the absence of ligand treatment, surface Ig in the B cell plasma membrane was fully dissolved by nonionic detergent; however, interaction with a ligand converted the receptor to a novel, detergent-insoluble state. The conversion of surface Ig to a detergent-insoluble form required receptor crosslinking but occurred independently of capping. Several types of experiments demonstrated that this form of Ig was not due to the size insolubility of immune complexes and involved a stable, noncovalent association of the receptor with the detergent-insoluble, cytoskeletal residue. Incubation of ligand-bound cells at 37 C promoted the degradation of surface Ig and the appearance of new, lower mw species, including a major soluble protein (50,000 daltons) that was antigenically related to surface Ig. These events corresponded to receptor endocytosis by several criteria (time course, temperature sensitivity, and energy dependence). Taken together, these results were consistent with the ligand-induced transmembrane attachment of receptors to the underlying cytoskeletal matrix followed by receptor internalization and catabolism. (Author abstract) (41 Refs)

## 21. RELATIONSHIP BETWEEN RECEPTORS FOR MOUSE ERYTHROCYTES AND MEMBRANE IMMUNOGLOBULINS IN NORMAL AND LEUKEMIC HUMAN LYMPHOCYTES.

Stollar A, Giraudo Conessa LC, Astaldi G

Departamento de Medicina Nuclear e Investigacion Inmunologica,, Instituto de Investigaciones Hematologicas Academia nacional de Medicina, Buenos Aires, Argentina

Medicina (B Aires); 41(Suppl):165-169 1981

Relationship between receptors for mouse RBC (MRBC) and membrane immunoglobulins (mIg) of peripheral lymphocytes in 10 healthy controls (HC: 50-70 yr old) and in 14 patients (similar distribution of sexes and age with the HC) with chronic lymphatic leukemia of B cell type (CLL-B) was studied. All the patients received therapy with corticosteroids and were divided into Group A (6 of the patients with lymphocytes less than 10,000/mm square) and Group B (8 with lymphocytes between 10,000-60.000/mm square). MRBC rosettes for HC were 8% +-2, for Group A were 33.17% +-23.3, and for Group B were 9.12% +- %.2. MRBC rosettes after incubation of lymphocytes with different antibodies were 6% +-3, 8.17% +-6.80, and 2.75% +-2.3, respectively, for anti Ig total. Values for anti IgM and anti IgG were similar to the values for anti Ig total, while anti IgD was 3% +-2, 11.17% +-7.6, and 2.75% +-3.90, respectively. Cells with mIg total were 17.5% +-5, 20.83% +-11.90, and 19.12% +-10.6, respectively; specific mIgM was 7.2% +-3.2, 11.83% +-9.4, and 5.37% +-4.8, respectively; specific mIgD was tested only for Group B and was 3.12% +-5, and specific mIgG was 10% +-4.5, 10.5% +-5.2, and 8.88% +-6.46, respectively. Relationships between the different values were considered and some hypotheses advanced. (23 Refs) (In SPA)

## 22. INVOLVEMENT OF HUMAN MEMBRANE-ASSOCIATED COMPLEMENT COMPONENTS IN THE ROSETTE FORMATION BETWEEN MARMOSET RED BLOOD CELLS AND HUMAN LEUKOCYTES.

Teillaud JL, Goujet-Zalc C, Fontaine M, Braun C, Mahouy G

Institut de Recherches sur les Maladies du Sang,, Laboratoire des Interactions lymphocytaires Hopital Saint-Louis, 75475 Paris Cedex 10, France

Cell Immunol; 66(2):254-268 1982

The majority of human monocytes, a subpopulation of B lymphocytes, and all but one B lymphoblastoid cell line (B-LCL) tested but one formed rosettes with Marmoset red blood cells (MaRBC). None of the human peripheral T cells, T-LCL, and B chronic lymphoid leukemia cells (B-CLL) used bind to MaRBC. The binding could not be correlated with any membrane markers or antigens present on cultured cells or peripheral blood leukocytes (PBL). Blocking of the rosette formation by preincubation of MaRBC with purified human complement (C) components and cobra venom or by pretreatment of leukocytes and cultured cells with antisera to human C components suggested that membrane-associated C components present on PBL or B-LCL are involved in the binding to MaRBC. (Author abstract) (35 Refs)

## 23. FC RECEPTORS OF MOUSE CELL LINES. II. IGG BINDING SPECIFICITY AND IDENTIFICATION OF THE FC RECEPTOR ON A LYMPHOID LEUKEMIA.

Lane BC, Bricker MD, Cooper SM

(c/o Cooper) Clinical Immunology and Rheumatic Disease Section, Univ. Southern California Sch. Medicine, 2025 Zonal Ave., HMR 711, Los Angeles, CA, 90033

J Immunol; 128(4):1825-1831 1982

We determined the binding specificity of the Fc receptors on the murine lymphoid leukemia, L1210, which bears several surface antigens characteristic of B cells and B cell precursors. L1210 possesses an Fc receptor that binds monomer IgG of the IgG1, IgG2a, and IgG2b subclasses with low affinity, whereas aggregated IgG of these subclasses is bound comparatively well. There was no detectable binding of monomer or aggregated IgG3. Although direct binding of monomer IgG was difficult to demonstrate, monomer inhibition of aggregate binding was found at monomer concentrations in excess of 0.2 mg/ml. There was cross-competition between monomers and aggregates of all three subclasses, indicating that all were binding to the same Fc receptor. Isolation and characterization of the Fc receptor of L1210 was accomplished by affinity chromatography of the radiolabeled cell lysate over columns of Sepharose 4B coupled to various IgG and control proteins. A single protein, with an approx mw of 60,000, was found to specifically bind to the Fc portion of IgG. This protein was demonstrated in the acetic acid and SDS eluates from columns coupled to monomer, aggregated, or antigen-complexed IgG, but was not seen in eluates from F(ab')2 columns or from eluates of IgG columns that received the lysates of Fc receptor-negative cells. The 60-kd Fc binding protein was also demonstrated in the SDS eluates from affinity columns of Sepharose 4B coupled to myeloma proteins of mouse IgG1, IgG2a, and IgG2b subclasses. These studies indicate that in contrast to mouse macrophage-like cell lines that possess separate IgG subclass specific Fc receptors, L1210, a murine leukemia of possible B cell lineage, possesses a single Fc receptor with distinct binding and structural characteristics. (Author abstract) (40 Refs)

## 24. DISTINCT FUNCTIONS OF SURFACE RECEPTORS IN THE INDUCTION OF NEUTROPHIL-MEDIATED CYTOTOXICITY.

Cordier G, Samarut C, Revillard JP

INSERM U. 80 and ERA-CNRS 782, Hopital E. Herriot, Pavillon P, 69374 Lyon Cedex 2, France

Ann Immunol (Paris); 132(1):3-14 1981

Roles of cell surface receptors for the Fc region of the IgG molecule, receptors for the activated third component of complement, and other undefined surface determinants of polymorphonuclear neutrophils (PMN) in the induction of cytotoxic activity towards heterologous target cells were investigated. The roles were studied in a model of cell-mediated cytotoxicity using 51Cr-labeled chicken erythrocytes as target cells and human PMN as effector cells. Results showed that the attachment of PMN to the target cell and the triggering of cytotoxicity are distinct events, and that hetero-antibodies against undefined PMN surface determinants can trigger the lysis of target cells attached to PMN. (27 Refs)

## 25. INTERFERON-INDUCED ANTIVIRAL ACTIONS IN FRIEND LEUKEMIA CELLS: ROLE OF MEMBRANE GANGLIOSIDES.

Belardelli F, Aliberti A, Santurbano B, Antonelli G, D'Agnolo G, Rossi GB

Servizio Biologico, Istituto Superiore di Sanita, Rome, Italy

Virology; 117(2):391-400 1982

The interactions between interferon (IFN) and membrane gangliosides have been analyzed in Friend leukemia cells (FLC). The GM1-cholera toxin (CT) model has been selected as a reference system for a high-affinity ganglioside-ligand binding. Two gangliosides have been detected in FLC extracts: a disialoganglioside (approx 95%) and a monosialoganglioside (approx 5%) which migrate respectively as GD1a and GM1. Unilammellar liposomes containing either mixed commercial gangliosides or GD1a or GM1 bind three to eight fold more IFN (both partially purified and pure) than gangliosides-free liposomes. Only 3-4% of the input IFN was bound, whereas GM1-containing liposomes bound almost 50% of [3H]acetyl-CT. Neuraminidase treatment of FLC, which converts GD1a-like into the GM1-like ganglioside, does not significantly modify the IFN-induced antiviral effects. CT binding to FLC as well as CT-induced elevation of endocellular cyclic AMP levels in FLC were instead markedly increased by the same neuraminidase treatment. Further, pretreatment of FLC with either GD1a or GM1 or gangliosides extracted from FLC did not change the IFN-induced establishment of the antiviral state. These data provide convincing evidence that FLC gangliosides do not represent the IFN high-affinity receptors nor specifically mediate IFN effects, even though they bind IFN to some extent. (Author abstract) (26 Refs)

## 26. ELECTROPHORETIC ANALYSIS OF RADIOLABELED CELL SURFACE PROTEINS AND GLYCOPROTEINS OF SOME HUMAN HEMOPOIETIC CELL LINES.

Chorvath B, Durej J, Stockbauer P, Babusikova O

Cancer Res. Inst., Slovak Acad. Sciences, 812 32 Bratislava, Czechoslovakia

Neoplasma; 28(6):625-632 1981

Cell surface proteins and glycoproteins of several human lymphoblastoid- and neoplastic hemopoietic cell lines were radiolabeled by lactoperoxidase catalyzed iodination and by sodium periodate/tritiated sodium borohydride. Electrophoretic patterns of radiolabeled proteins and glycoproteins obtained by electrophoresis under denaturing conditions (SDS-PAGE) were essentially similar for all examined lymphoblastoid cell lines, with a characteristic group of major radiolabeled glycoproteins gp44 and gp24,31. Characteristic, individually different and distinguishable patterns of radiolabeled proteins were observed in different neoplastic hemopoietic cell lines: T-leukemia cell line MOLT 3, erythroleukemic cell line K562, pre-B cell leukemia line NALM 6, and a promyelocytic leukemia cell line HL-60. Cell surface proteins of HL-60 promyelocytic leukemia cell line displayed some similarities to those of another myeloid leukemia cell line ML 3. Examined Burkitt lymphoma cell lines were similar to lymphoblastoid cell lines with some minor differences. Glycoprotein gp44, markedly labeled on lymphoblastoid cell lines, was absent on Burkitt lymphoma cell line Daudi. Electrophoretic patterns of cell surface proteins of blast cells from a few patients with leukemia examined simultaneously with the cell lines are described and discussed. (Author abstract) (28 Refs)

# LYMPHOCYTE AND DIFFERENTIATION ANTIGENS

## 27. MONOCLONAL ANTIBODIES OKT 11 AND OKT 11A HAVE PAN-T REACTIVITY AND BLOCK SHEEP ERYTHROCYTE 'RECEPTORS'.

Verbi W, Greaves MF, Schneider C, Koubek K, Janossy G, Stein H, Kung P, Goldstein G

(c/o Greaves), Imperial Cancer Res. Fund, P.O. Box 123, Lincoln's Inn Fields, London WC2A 3PX, England

Eur J Immunol; 12(1):81-86 1982

Monoclonal antibodies OKT11 (gamma1) and OKT11A (gamma2) are described and appear to have similar binding specificities. They bind, in immunofluorescence, with greater than 95% of infant thymocytes, staining both cortical and medullary cells, 65-80% of blood lymphocytes and selectively stain the T cell-dependent paracortical areas of tonsil. A small proportion (9-12%) of bone marrow lymphocytes stain, but this population excludes the terminal transferase-positive cells. Both the gamma1 and gamma2 antibodies stain the surface membrane Ig-negative lymphocytes in blood and tonsil and are able to block sheep E rosette formation (to normal or leukemic T cells). In contrast, other monoclonal anti-T reagents tested (OKT1, OKT3, OKT4, OKT6, OKT8, OKT9, OKT10) did not block E rosette formation. E rosette formation and OKT11 binding are coincident on T-ALL cell lines and both are trypsin-sensitive. In a series of 145 leukemias and 26 leukemic cell lines investigated, only leukemias with a T cell phenotype including E rosette positivity were reactive with OKT11 and OKT11A. OKT11A binds to a polypeptide of approx 50,000 molecular wt on thymic lymphocytes. This structure may carry the recognition site for sheep erythrocytes. These antibodies provide additional useful markers for T cell analysis and are of potential therapeutic value. (Author abstract) (25 Refs)

## 28. EXPRESSION OF QAT-4 AND QAT-5 ALLOANTIGENS ON CYTOTOXIC PRECURSOR AND EFFECTOR CELLS: DIFFERENT SURFACE PHENOTYPES OF ALLOREACTIVE AND H-2-RESTRICTED CYTOTOXIC T CELLS.

Zahn G, Hammerling GJ, Eichmann K, Simon MM

(c/o Simon), Max-Planck-Institut fur Immunobiologie, Postfach 1169, D-7800 Freiburg, W. Germany

Eur J Immunol; 12(1):43-50 1982

Monoclonal anti-Qat-4 and anti-Qat-5 antibodies, which define antigens expressed on peripheral T cell subsets, have been used to study the phenotypes of alloreactive and H-2-restricted cytotoxic effector cells and their precursors. Depletion of Qat-4+ or Qat-5+ cells from the T cell pool prior to their sensitization in bulk cultures prevented the development of alloreactive and H-2-restricted cytotoxic activities in the selected populations. No reconstitution of cytolytic activities to normal levels was obtained when mixtures of Qat-4 and Qat-5-cells were sensitized in bulk cultures to H-2 or non-H-2 antigens. Sensitization of limiting numbers of Qat-4-or Qat-5-lymphocytes under optimal conditions for help (interleukin 2), with the appropriate antigens (H-2, H-Y) did not result in the generation of cytotoxic T cells, indicating that the majority of all cytotoxic T lymphocyte (CTL) precursors are Qat-4+, Qat-5+. When CTL effector populations were treated with the antisera and complement (C) at their maximum CTL activity, it was found that H-2-restricted CTL were totally eliminated by anti-Qat-4 and considerably reduced by anti-Qat-5 antisera and C. In contrast, alloreactive CTL effector cells were insen-

sitive to anti-Qat-4 and to anti-Qat-5 plus C. Although alloreactive CTL effector populations regained some Qat-4 antigens during further in vitro culture, it was shown that H-2-restricted CTL were at all times more sensitive to anti-Qat-4 than were alloreactive CTL. The findings suggest that during maturation of alloreactive and H-2-restricted CTL from their precursors, both alloantigen undergo differential quantitative variations in the ir expression that lead to different Qat-4,5 phenotypes of alloreactive and H-2-restricted CTL. (Author abstract) (20 Refs)

### 29. BIOCHEMICAL CHARACTERISATION OF LEUKAEMIA-ASSOCIATED ANTIGEN P24 DEFINED BY THE MONOCLONAL ANTIBODY BA-2.

**Newman RA, Sutherland DR, Lebien TW, Kersey JH, Greaves MF**
**Membrane Immunology Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England**
**Biochim Biophys Acta; 701(3):318-327 1982**

The leukemia-associated cell surface antigen p24/BA-2 is a single polypeptide chain with a molecular wt of 24,000. Treatment with glycosidases or exposure of cells to tunicamycin failed to show any change in the mol wt of the antigen when examined by SDS-polyacrylamide gel electrophoresis. In addition, it failed to bind to lectin affinity columns of concanavalin A, lentil lectin or Ricinus communis lectin. This is consistent with the absence of N-asparagine linked oligosaccharide chains on the antigen. Pulse-chase labeling of protein p24 shows a post-translational modification resulting in a mol wt increase of approx 500-1,000. Alkaline treatment resulted in a decrease in mol wt of approx the same amount, suggesting that p24 may contain some O-glycosidically linked oligosaccharide. Protein p24 has a basic pI of 7.3 which is unchanged after neuraminidase treatment. Protein p24/Ba-2 cannot be labeled by either the lipophilic photoactivatable nitrene reagent, hexanoyldiiodo-N-(4-azido-2-nitrophenyl)tyramine, or with [32P]phosphate. This suggests that the molecule is non-integral in nature and that it does not form an intimate association with the lipid matrix. Identical mol wt, when reduced and non-reduced antigens were compared, suggest that it contains no internal disulfide linkages and failure to detect any other band on gradient gel SDS-polyacrylamide gel electrophoresis from 5-15% suggests that it is not strongly associated with any other structure. (Author abstract) (31 Refs)

### 30. PERSPECTIVES: IA SPECIFICITIES IN MOUSE AND MAN.

**McKenzie IF, Sandrin MS, Parish CR**
**Dept. Medicine, Austin Hosp., Heidelberg, Victoria 3084, Australia**
**The Handbook of Cancer Immunology: Volume 8- Tumor Antigens: Structure and Function. Waters H, ed. New York, STPM Garland Press, 418 pp., 1981.**

Two types of Ia antigen, in a limited tissue distribution, have been found in both mice and humans: a glycoprotein (Ia+ GLP; mol wt about 30,000) and a low mol wt glycolipid (Ia+ GLL). Both fractions are present on B-lymphocytes, a subpopulation of T-lymphocytes, a subpopulation of null cells, and macrophages. High levels of Ia+ GLL are also present in the serum; the concentration reflects the degree of T-cell activation. In both species, serum Ia+ GLL levels decline severely in the presence of a growing malignant tumor. Studies on the Ia antigen region of the major histocompatibility complex (MHC) of mice s howed that the serum Ia+ GLL component is produced by Ia- T-lymphocytes (surface phenotype: Thy-1+ Ly-1+ Ly-2+). Anti-Ia antibodies appeared in an animal rejecting a mammary carcinoma (A.TL) of Ia- surface phenotype, suggesting that the tumor may have secreted Ia antigens. These Ia molecules (possibly GLL) might interact with other molecules (either Ia+ GLL or GLP), leading to the suppression of host GLL production. These phenomena may be related to the altered cell surface GLL patterns observed in tumors. The I region of the MHC and the Ia antigens are probably involved in the immune response to tumors, as they seem to be involved in all or most immune reactions. It is suggested that the Ia+ GLL may play a particularly important role in oncogenesis. (194 Refs)

### 31. GENETIC AND REGULATORY CONTRIBUTIONS OF THE MAJOR HISTOCOMPATIBILITY COMPLEX TO THE DEVELOPING CYTOLYTIC T LYMPHOCYTE REPERTOIRE.

**Sherman LA**
**Dept. Immunopathology, Scripps Clinic and Res. Foundation, 10666 North Torrey Pines Road, La Jolla, CA, 92037**
**J Immunol; 128(4):1849-1853 1982**

The specificity repertoire of H-2Kb-specific CTL derived from 10-to 14-day-old neonates was examined. Analogous to the adult repertoire, the neonatal repertoire is composed of a large number of receptor specificities, each of which is represented at a low frequency, as well as a small number of highly recurrent specificities, which thereby serve as repertoire markers. The expression of most specificities appears to be independently regulated during development, resulting in the expression of a different set of recurrent specificities for neonates and adults within the same strain. The neonatal and adult repertoires were also compared with respect to the influence of the MHC on repertoire. Unlike adults, neonates of MHC different congenic strains (B10.D2 and B10.BR) have in common approx half their recurrent specificities. Additionally, most parental specificities are expressed codominantly in neonatal F1 hybrids. These results may be interpreted as indicating either that (1) some, but not all, receptor genes demonstrate MHC-linked polymorphism and both parental alleles are expressed in F1 neonates, or (2) T receptor genes are nonpolymorphic in MHC congenic strains and the observed MHC-related repertoire differences are attributable to a positive selection mechanism. Since adults of these same strains so not display significant repertoire similarity, it is suggested that this increased repertoire divergence may be the result of encounters with environmental antigens in association with self-MHC antigens. (Author abstract) (24 Refs)

### 32. BIOSYNTHESIS AND PROCESSING OF A HUMAN T LYMPHOCYTE ANTIGEN.

**Bergman Y, Levy R**
**Howard Hughes Medical Inst., Stanford Univ., Stanford, CA, 94305**
**J Immunol; 128(3):1334-1340 1982**

The biosynthesis and processing of Leu-1, a human T lymphocyte antigen, has been studied with the use of a monoclonal antibody. This molecule exists on the cell surface as a 67,000 mw glycoprotein. Through a series of pulse-labeling studies, in conjunction with the use of the antibiotic tunicamycin and the enzyme Endo-H, the details of glycosylation, processing, and deposition at the cell membrane were examined. The protein backbone of the molecule is 58,000 mw. High-mannose sugars are added to asparagine residues during synthesis. Within 20 min, these high mannose sugars are converted to complex type carbohydrates, including fucose. The fully processed glycoprotein appears at the cell surface within 30 min after synthesis. This sequence of events is similar to that for other cell surface

glycoproteins, including HLA and vesicular stomatitis virus glycoprotein. (Author abstract) (35 Refs)

### 33. INHIBITION OF MURINE T CELL-MEDIATED CYTOLYSIS AND T CELL PROLIFERATION BY A RAT MONOCLONAL ANTIBODY IMMUNOPRECIPITATING TWO LYMPHOID CELL SURFACE POLYPEPTIDES OF 94,000 AND 180,000 MOLECULAR WEIGHT.

Pierres M, Goridis C, Golstein P
Centre d'Immunologie, INSERM-CNRS de Marseille-Luminy, Case 906, F-13288 Marseille Cedex 9, France
Eur J Immunol; 12(1):60-69 1982

The monoclonal antibody methodology was used to identify membrane structures involved in T cell functions. To optimize chances to produce and detect relevant antibodies, a xenogeneic sensitization protocol was utilized and hybridoma supernatants were screened, on functional rather than structural grounds, for their ability to inhibit a given function. The test function was T cell-mediated cytolysis. Mouse cytolytic anti-allogeneic cell populations were used to sensitize a rat, the spleen cells of which were fused to produce hybridomas; the supernatants of the latter were screened for their ability to inhibit mouse T cell-mediated cytolysis in vitro. Several inhibitory antibodies were obtained, one of which, H35-89.9 monoclonal antibody, was studied in more detail. It inhibited specific and concanavalin A (Con A)-mediated cytolysis by T cells, by acting on the effector cells. it reversibly inhibited soluble antigen-, alloantigen and Con A-induced T cell proliferation (but not LPS-induced B cell proliferation), after the production of interleukin 2, by acting on the responder cells. It also had a disagglutinating effect on Con A and LPS blasts and on EL4 cells. It immunoprecipitated from thymocyte membrane preparations two structures of 94,000 and 180,000 apparent molecular wt, and recognized cell surface determinants on both T and B lymphocytes. Our findings suggest that several antibodies directed against distinct effector cell membrane structures inhibit cytolysis. The case of H35-89.9 monoclonal antibody, which exerts multiple functional effects and immunoprecipitates two membrane polypeptides, raises the problem of the various possible relationships between t hese structures and functions. (Author abstract) (48 Refs)

### 34. COMPLEXITY OF THE HUMAN T LYMPHOCYTE-SPECIFIC CELL SURFACE ANTIGEN T3.

Borst J, Prendiville MA, Terhorst C
Div. Tumor Immunology, Sidney Farber Cancer Inst., 44 Binney Street, Boston, MA, 02115
J Immunol; 128(4):1560-1565 1982

A human T lymphocyte cell surface antigen T3 was found to be involved in several functions that were specific for the cells that express this marker on their surface. We show here that several glycoproteins were found in the immunoprecipitates prepared with a monoclonal reagent anti-T3. In addition to the major glycoprotein complex of 20 kd, glycoproteins of 25 to 28 kd, 37 kd, and 44 kd were detected in immunoprecipitates. The charge heterogeneity of the 20 kd and 25 to 28 kd proteins was caused by variable sialic acid content. The 20-kd T3 glycoprotein carried several 'complex-type' and endoglycosidase-H-sensitive sugar moieties. We found that the 20-kd protein could be labeled with 125I-iodonaphthylazide, a reagent that reacts with hydrophobic areas of proteins. (Author abstract) (24 Refs)

### 35. ALTERATION OF LYMPHOID CELLS IN AKR MICE BY TREATMENT WITH MONOCLONAL ANTIBODY AGAINST THY-1 ANTIGEN.

Tam MR, Bernstein ID, Nowinski RC
Genetic Systems Corporation, 3005 First Ave., Seattle, WA, 98121
Transplantation; 33(3):269-273 1982

AKR/J mice treated with high levels of monoclonal anti-Thy-1.1 antibody and C' remained healthy without apparent side effects. Examination of the lymphatic organs of these mice demonstrated a selective depletion of T cells in lymph nodes and spleen. Following cessation of treatment of the levels of anti-Thy-1.1 antibody in the circulation fell and the peripheral lymphatic organs gradually became repopulated with T cells. Depletion occurred in lymph nodes whether or not C' was infused along with the antibody. Although the thymocytes of these mice were coated with anti-Thy-1.1 antibody they were not eliminated by the treatment. The elimination of peripheral but not thymic T cells suggests either a thymic barrier to the penetration of cofactors (possibly antibody-dependent effector cells) or that antibody acts by interfering with the normal traffic of peripheral T cells which normally 'home' to the lymph nodes and spleen. (Author abstract) (9 Refs)

### 36. A MONOCLONAL ANTIBODY DETECTING UNUSUAL THY-1 DETERMINANTS.

Auchincloss H, Ozato K, Sachs DH
Transplantation Biology Section, Immunology Branch, NCI, NIH, Bethesda, MD, 20205
J Immunol; 128(4):1584-1589 1982

The substance 20-10-5S is a monoclonal antibody produced by the fusion of C3H anti-C3H.SW splenocytes with the SP2/0 cell line. The antibody appears to react with Thy-1 determinants by several criteria including cytotoxicity patterns, functional assays, genetic analyses, and competitive bind ing experiments. However, the antibody and the determinants it detects are unusual in that: (1) 20-10-5S is autoreactive; (2) the antibody shows allospecificity for Thy-1.2 vs Thy-1.1 antigens only on peripheral lymphocytes and not on the thymocytes; and (3) the antibody reacts only with determinants on murine T cells and not with antigens on brain tissue or on rat thymocytes. It therefore seems that 20-10-5S reacts with murine T cell-specific Thy-1 determinants that are lost or modified during maturation of the cells on which they are expressed. (Author abstract) (23 Refs)

### 37. SURFACE MARKERS OF CLONED HUMAN ALLOREACTIVE T LYMPHOCYTES.

Chardonnens X, Froment Y, Joye MT, Jeannet M
Transplantation Immunology Unit, Div. Immunology and Allergology, Hopital Cantonal Universitaire, Geneva, Switzerland
Immunogenetics; 15(3):327-330 1982

Surface markers (SM) of cloned T cells are reviewed and their correlation with T cells functional activity is discussed. SM and proliferative and cytolytic activity of cloned effector cells are tabulated. Cytolytic or primed lymphocyte test (PLT) reactive clones could not always be clearly distinguished from unreactive clones by their SM. Six of seven clones with cytolytic activity against the original stimulator had the OKT8 marker and none of them reacted with the OKT4 reagent. The OKT4 marker was detected on three noncytolytic clones, two of which were reactive in the PLT assay. One OKT4 clone was lytic for K562 cells. (11 Refs)

## 38. CELLULAR REGULATION OF GAMMA INTERFERON PRODUCTION: LYT PHENOTYPE OF THE SUPPRESSOR CELL.

Torres BA, Yamamoto JK, Johnson HM
Dept. Microbiology, Univ. Texas Medical Branch, Galveston, TX, 77550
Infect Immun; 35(3):770-776 1982

Suppressor cell activity for in vitro gamma interferon (IFN-gamma) production can be induced in C57BL/6 mice with staphylococcal enterotoxin A and concanavalin A. The suppressor cell lacked mitogen specificity. The IFNgamma-producing cell has a low density of Thy 1. Monoclonal anti-Lyt 2.2 antibody completely eliminated the suppressor cell activity, whereas anti-lyt 1.2 partially reduced the suppressor cell activity. The suppressor cell may be or may require a Lyt 1,2,3+ cell with a relatively low density of the Lyt 1 antigen for activity. Treatment of cells with either anti-Lyt 1.2 or anti-Lyt 2.2 completely eliminated IFNgamma production in both virgin and suppressor cell cultures. Cocultivation of Lyt 1+ and Lyt 2+ cells in both virgin and suppressor cell cultures restored the ability to produce IFNgamma when cells were stimulated with staphylococcal enterotoxin A. For the virgin cells, this seems to indicate clearly that both Lyt 1+ and Lyt 2+ cells are required for IFN production, but that Lyt 1,2,3+ cells are not required. For the suppressor cell population this type of treatment resulted in IFNgamma production comparable to that of the virgin cell population. The treatment eliminated or depleted Lyt 1,2,3+ cells from the suppressor cell population, thus providing additional evidence that a Lyt 1,2,3+ cell is required for suppressor cell activity. Treatment of spleen cells with anti-Lyt antibodies at the time that they were involved in ongoing IFNgamma production showed that the IFNgamma-producing cell is Lyt 2+. A 1:1 ratio of virgin to suppressor cells was required for suppression of IFNgamma production by virgin spleen cells. Preliminary data showed that the suppressor cell activity could be induced in in vitro cultures incubated with mitogen for 4 days. This is evidence that the suppressor cell is inducible and not necessarily recruited to the spleen from other lymphoid organs. (Author abstract) (22 Refs)

## 39. INACTIVATION OF STEM CELLS BY ALLOGENEIC LYMPHOCYTES: CHARACTERISTICS OF SUPPRESSOR CELLS BLOCKING THE KILLER EFFECT OF SYNGENEIC LYMPHOCYTES.

Ignat'eva GA, Man'ko VM, Dishkant IP
Moscow, USSR
Tsitologiia; 23(12):1386-1394 1981

Mechanism of interaction of killer and suppressor cells was studied in CBA, C57BL, and (CBA x C57Bl)F1 mice. Analysis of inactivating ability of different subpopulations of T-lymphocytes showed that the killer activity of T lymphocytes from the lymph nodes (T-LN) was similar to that of T-lymphocytes from the spleen (T-S) if the total number of transplanted cells did not exceed 5 x 10(5). For larger doses of transplanted cells, the killer activity of T-LN was greater than that of T-S. Index of inactivation of the stem cells after transplantation of a mixture of T-LN and T-S was less than the sum of inactivation indices for T-LN alone and T-S alone. Interaction of T-LN and T-S depended upon the ratio of lymphoid components in the mixture. Antilymphocytic sera inhibited killer cells but did not affect suppressor cells. In vitro experiments showed that killer cells belong to anti-Thy-1-sensitive T-lymphocytes. Suppressor cells were found to be resistant to anti-Thy-1-sera. The spleen cells from thymectomized mice did not exhibit the suppressor activity. Thymectomy did not affect activity of killer cells. (15 Refs) (In RUS)

## 40. BIOCHEMICAL CHARACTERIZATION AND CELLULAR DISTRIBUTION OF A POLYMORPHIC, MURINE CELL-SURFACE GLYCOPROTEIN EXPRESSED ON LYMPHOID TISSUES.

Trowbridge IS, Lesley J, Schulte R, Hyman R, Trotter J
Dept. Cancer Biology, Salk Inst., Post Office Box 85800, San Diego, CA, 92138
Immunogenetics; 15(3):299-312 1982

A murine leukocyte surface glycoprotein (Mr = 95,000) has been defined by means of xenogeneic monoclonal antibodies. In normal hematopoietic tissues, the glycoprotein is found in highest amounts in the bone marrow. Flow cytometric analysis shows that essentially all bone-marrow cells express the glycoprotein and that it is a major component of a subpopulation of cells containing predominantly granulocytic precursors. In contrast, only about 5% of thymocytes express sufficient glycoprotein to be detected by flow cytometric analysis, although under stringent conditions up to 20% of thymocytes are susceptible to complement-mediated cytotoxicity using a monoclonal antibody against the glycoprotein. Functional assays showed that both prothymocytes and colony forming unit-spleen express the glycoprotein which is broadly distributed on murine hematopoietic tumor cell lines. However, although some Thy-1+ (T) cell lymphomas express large amounts of the glycoprotein, others do not express detectable quantities of the molecule. The glycoprotein is not restricted to hematopoietic cells and can be detected on lung, kidney, brain, and liver as well as cultured fibroblasts. Monoclonal antibodies against the glycoprotein cross-react with an antigen present on human cells. As described in the accompanying paper, the glycoprotein exists in two antithetical allelic forms and we show that it is identical to a polymorphic surface molecule independently characterized by Colombatti and co-workers. (Author abstract) (41 Refs)

## 41. GENETIC CHARACTERIZATION OF A POLYMORPHIC MURINE CELL-SURFACE GLYCOPROTEIN.

Lesley J, Trowbridge IS
Dept. Cancer Biology, Salk Inst., Post Office Box 85800, San Diego, CA, 92138
Immunogenetics; 15(3):313-320 1982

As described in the preceding paper, monoclonal antibodies have been raised by immunization of rats with mouse hematopoietic cells which detect a major cell-surface glycoprotein (Mr = 95,000) of mouse bone-marrow cells of the granulocytic series. While most of the monoclonal antibodies detect this molecule on bone-marrow and spleen cells of all mouse strains, two antibodies recognize alternative allelic forms of the molecule. One alloantigen is expressed in all the remaining inbred strains examined. The alloantigens are codominantly expressed on the cells of F1 mice. Backcrosses of DBA/2 and C57BL/6 with F1 mice (B6D2F1) confirmed that a single genetic locus is involved in the expression of the two antigenic forms and demonstrated linkage to Ly-m11 which has previously been mapped to mouse chromosome 2. These genetic mapping experiments and the biochemical properties of the glycoprotein suggested that it might be identical to a glycoprotein first identified on murine fibroblasts by Hughes and August and designated Pgp-1. This has been firmly established by exchange of monoclonal antibody reagents and sequential immunoprecipitations. (Author abstract) (16 Refs)

### 42. A GENERAL METHOD FOR THE CYTOCHEMICAL AND ULTRASTRUCTURAL STUDIES OF HUMAN LYMPHOCYTE SUBSETS DEFINED BY MONOCLONAL ANTIBODIES.

Bernard J, Terraynck T, Zagury D
Institut Jean-Godinot, 51100 Reims, France
Immunol Lett; 4(2):65-73 1982

A method of general applicability is described for further characterization of lymphocyte subsets as defined by monoclonal antibodies. Human lymphocyte subpopulations were identified by means of anti-mouse immunoglobulin (Ig)-coated latex microspheres or ox RBC following treatment with mouse hybridoma antisera specific for differentiation markers on the surface of T- or B-cells. Optimal conditions are described for a panel of monoclonal mouse hybridoma antisera from various sources. The method is as sensitive as the complement-mediated microcytotoxicity assay, is rapid, easy to perform and permits exhaustive light and electron microscopic studies of lymphocytes bound to the carrier particles. Correlation between membrane differentiation antigens detected by monoclonal antibodies and intracellular enzyme markers established by cytochemical treatment of rosettes can provide additional data on the association of membrane and cytoplasmic lymphocyte markers and possibly reveal discrete stages of lymphoid cell maturation and provide information on the classification of neoplastic lymphocytes. (18 Refs)

### 43. MAC-2, A NOVEL 32,000 M4 MOUSE MACROPHAGE SUBPOPULATION-SPECIFIC ANTIGEN DEFINED BY MONOCLONAL ANTIBODIES.

Ho MK, Springer TA
Lab. Membrane Immunochemistry, Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115
J Immunol; 128(3):1221-1228 1982

Two monoclonal antibodies, M3/31 and M3/38, were obtained by fusion of mouse myeloma cells with rat spleen cells immunized to immunoadsorbent-purified macrophage glycoproteins. Co-precipitation experiments show that antigenic determinants recognized by these two antibodies reside on the same molecular species, termed Mac-2. Mac-2, an antigen of 32,000 Mr, is synthesized by and expressed on the surface of thioglycollate-elicited macrophages as shown by [35S]-methionine and 125I labeling. Saturation binding experiments show that thioglycollate-elicited macrophages express 1.7 x 10(5) Mac-2 sites/cell. Thioglycollate-elicited macrophages are strongly absorptive for 125I-labeled M3/38 MAb. Kidneys are also absorptive; however, evidence is presented pointing to the nonspecificity of this absorption. Lymph node and thymus are negative, whereas spleen and bone marrow are weakly absorptive, probably due to stromal cells. Nonlymphoid tissues, such as lung, liver, heart, and brain, exhibit slight or no absorbing capacity. Cell suspensions from spleen, bone marrow, thymus, and peripheral lymph node are greater than 99% Mac-2-by immunofluorescent flow cytometry. In contrast, thioglycollate-elicited macrophages are greater than 96% strongly positive for Mac-2. Only 20% of peptone-elicited cells are weakly positive, whereas resident peritoneal macrophages and other macrophages elicited by Listeria monocytogenes, Con A, or LPS are greater than 98% negative. SDS-PAGE of [35S]-methionine-labeled Mac-2 shows that thioglycollate-elicited macrophages synthesize 10-to 30-fold more Mac-2 than other peritoneal macrophage subpopulations, whereas all types of peritoneal macrophages synthesize and express on their surfaces similar amounts of the Mac-1 antigen. Mac-2 antigen is therefore induced in macrophages only in response to specific differentiative signals. (Author abstract) (30 Refs)

### 44. FUNCTIONALLY DIFFERENT SUBPOPULATIONS OF MOUSE MACROPHAGES RECOGNIZED BY MONOCLONAL ANTIBODIES.

Sun D, Lohmann-Matthes M
Max-Planck-Institut fur Immunobiologie, Postfach 1169, D-7800 Freiburg, W. Germany
Eur J Immunol; 12(2):134-140 1982

Four rat anti-mouse macrophage monoclonal antibodies are described. Three of them are highly specific for macrophages, and one cross-reacts with granulocytes. All four antibodies do not react with membrane antigens shared by all macrophages, but with antigens present only on subpopulations of 20-50% of the cells. All antibodies are directly or indirectly cytotoxic for macrophages. The subpopulations defined by these antibodies can be correlated with certain macrophage functions. Thus, antibody M43 eliminates macrophages that are activated by lymphokine to cytotoxicity. Antibodies M43 and M57 eliminate macrophages that kill antibody-coated tumor targets, and clone 102 (strictly macrophage-specific) eliminates natural killer cells. Only M143, reacting with 10-30% of macrophages, has not yet been correlated with any function. With the use of these antibodies, cells of the macrophage lineage with specific functions can be recognized and eliminated for a given population. (Author abstract) (22 Refs)

## CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION

### 45. PHORBOL ESTER-INDUCED DIFFERENTIATION OF A NON-T, NON-B LEUKEMIC CELL LINE: MODEL FOR HUMAN LYMPHOID PROGENITOR CELL DEVELOPMENT.

LeBien TW, Bollum FJ, Yasmineh WG, Kersey JH
Dept. Lab. Medicine and Pathology, Univ. Minnesota, Box 609 Mayo, Minneapolis, MN, 55455
J Immunol; 128(3):1316-1320 1982

The phorbol ester 12-O-tetradecanoylphorbol-13-acetate (TPA) was tested for its ability to induce phenotypic changes in the human non-T, non-B ALL cell line REH. Cells were cultured with nanogram concentrations of TPA for up to 48 hr, and were analyzed by indirect immunofluorescence with a panel of monoclonal antibodies and an antibody to the enzyme terminal deoxynucleotidyl transferase (TdT). TPA induced REH cells to express the leukemia-associated antigen, p24 (detected with monoclonal antibody BA-2; p24/BA-2) by 8 hr of culture, with induction complete by 24 hr. TPA-treated cells also underwent a concomitant decrease in the expression of TdT when analyzed enzymatically or by immunofluorescence. Analysis of TPA-treated cells with monoclonal antibodies BA-1 (detecting a B cell-associated antigen), 7.2 (detecting a monomorphic HLA-DR antigen), or OKT11 (detecting a structure closely associated with the E receptor) showed no change compared to controls. In addition there was no detectable cytoplasmic immunoglobulin in control or TPA-treated cells. These results show clearly that TPA is capable of inducing phenotypic changes in REH cells. Such changes may reflect the differentiation-linked expression of antigens present in normal bone marrow lymphoid progenitor cells. (Author abstract) (41 Refs)

## 46. INDUCTION OF MATURATION IN CULTURED HUMAN MONOCYTIC LEUKEMIA CELLS BY A PHORBOL DIESTER.

Tsuchiya S, Kobayashi Y, Goto Y, Okumura H, Nakae S, Konno T, Tada K
Dept. Pediatrics, Tohoku Univ. Sch. Medicine, Sendai 980, Japan
Cancer Res; 42(4):1530-1536 1982

Suspension cultures of a human monocytic leukemia cell line, THP-1, were treated with 0.16 to 160 nM 12-O-tetradecanoylphorbol-13-acetate (TPA). In an original cell line, THP-1-O, cultured again from-80 C cryopreservation, more than 80% of the cells adhered to the glass substrate with marked morphological change within 3 hr of TPA treatment. Adherent cells became flat and ameboid in shape, and many microvilli and flaps of the cell surface disappeared. Well-developed Golgi apparatus, rough endoplasmic reticula, and a large amount of free ribosomes were seen in the cytoplasm. On the other hand, in THP-1-R cells cultured continuously without cryopreservation for 26 mo, approximately 80% of the cells adhered to the substrate 48 hr after TPA treatment. Round and ovoid shapes were kept in THP-1-R cells treated with TPA. Surface Fc receptors for immunoglobulin G were present on more than 90% of THP-1-O and THP-1-R cells and were little affected by treatment with TPA. Sixty to 70% of the TPA-treated THP-1-O and THP-1-R cells were able to phagocytize yeasts and immunoglobulin G-coated sheep erythrocytes. Less than 20% of the untreated THP-1 cells were able to phagocytize yeasts and immunoglobulin G-coated sheep erythrocytes. In histochemical staining, alpha-naphthyl butyrate esterase was enhanced after treatment with TPA. Lysozyme activity in culture supernatants was not affected by TPA treatment. When exposed to latex beads and TPA, increased 14CO2 production from [1-14C]glucose in THP-1-O cells was observed. These results indicate that, after treatment with TPA, human monocytic leukemia cells may be converted into mature cells with functions of macrophages. (Author abstract) (24 Refs)

## 47. DEXAMETHASONE SYNERGISTICALLY INDUCES CHEMOTACTIC PEPTIDE RECEPTOR EXPRESSION IN HL-60 CELLS.

Skubitz KM, Zhen YS, August JT
Dept. Medicine, Johns Hopkins Univ. Sch. Medicine, 725 North Wolfe St., Baltimore, MD, 21205
Blood; 59(3):586-593 1982

We have examined the effect of physiologic concentrations of dexamethasone on th e induction of differentiation of the human promyelocytic leukemia cells (HL-60) and the activity of surface receptors for the f-met-leu-phe chemotactic peptide. Dexamethasone at a concentration of 500 nM was markedly synergistic with dimethylformamide and dimethylsulfoxide, but not with trans-retinoic acid, in inducing f-met-leu-phe binding by HL-60 cells. The increase in peptide binding was due to an increase in the activity of peptide receptors rather than an increase in receptor affinity. The effect of dexamethasone was relatively specific for peptide binding as there was little effect when HL-60 differentiation was assessed by cell morphology or the ability of the cells to reduce nitroblue tetrazolium. Dexamethasone alone had no reproducible effect on HL-60 differentiation as assessed by the three criteria tested. The dexamethasone concentration required for half maximal synergism correlated with the known binding constant of the hormone for steroid receptors in HL-60 cells but the effect of dexamethasone was not blocked with the steroid blocking agents 17 alpha methyltestosterone or progesterone. (Author abstract) (42 Refs)

## 48. REGULATION OF MACROPHAGE POPULATIONS. IV. MODULATION OF IA EXPRESSION IN BONE MARROW-DERIVED MACROPHAGES.

Calamai EG, Beller DI, Unanue ER
Dept. Pathology, Harvard Medical Sch., Boston, MA, 02115
J Immunol; 128(4):1692-1594 1982

The expression of I region-associated (Ia) antigens was studied in macrophages derived from bone marrow cell precursors cultured in L cell-conditioned medium (LCM) as a selective growth stimulator. Very few macrophages expressed Ia either while growing actively in LCM or when quiescent, after the removal of LCM from the culture. The addition of T cell lymphokines, however, stimulated the biosynthesis and membrane expression of Ia. Uptake of bacteria by the macrophage during exposure to the lymphokines produced a synergistic increase in Ia expression. The lymphokine-induced stimulation of Ia was reduced by the simultaneous presence of LCM, suggesting that growth and differentiative stimuli have opposing effects on Ia induction. All macrophage colonies derived from single precursors contained cells that could be induced to express Ia. (Author abstract) (15 Refs)

## 49. ANTIBODY AND B CELL REGULATION OF IMMUNITY.

Gilbert K, Hoffmann MK
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
The Handbook of Cancer Immunology: Volume 9- Humoral Immunity in Relation to Cancer. Waters H, ed. New York, Garland STPM Press, 289 pp., 1981.

Antibody (Ab) formation by B-lymphocytes depends on a sequence of coordinated interactions of the B-cells with helper T-lymphocytes and macrophages. Antigen (Ag), binding to the surfaces of T- or B-cells (specifically) or macrophages (nonspecifically), may act as a triggering signal and a bridge between Ag-reactive cells. Ag-mediated bridging of B-cells and helper cells is sensitive to negative feedback control by Ab, apparently by two mechanisms. One mechanism, requiring high Ab levels, is based on the masking of Ag determinants, leaving them inaccessible to responsive lymphocytes. The other mechanism, operative in the presence of low Ab levels, presumably interferes with B-/helper cell cooperation without affecting Ag recognition by the immunocytes. The Ab-mediated inhibition of Ab production is reversible in factors present in tumor necrosis serum, which replaces helper T-cells and macrophages. An Ab may interfere with the appropriate B-/helper cell interaction by binding Ab may interfere with the appropriate B-/helper cell interaction by binding Ag via its Fc receptor (FcR) to FcR-containing (FcR+) cells, where the Ag is accessible to recognition by immunocytes but incapable of directing the appropriate association of B-cells with helper cells. Two mechanisms of Ab-mediated inhibition seem to be involved in cell-mediated immune reactions to tumors. One mechanism involves the masking by Ab of tumor Ag determinants. The other mechanism involves the formation of Ag-Ab complexes. It is suggested that the Ab may bind (via its Fc portion) a solubilized tumor Ag to the surfaces of FcR+ cells, thus diverting the cytotoxic lymphocytes from their tumor cell targets. (110 Refs)

## 50. INTERACTIONS BETWEEN LYMPHOCYTE MEMBRANE MOLECULES. II. CHARACTERIZATION OF AN INTERACTION BETWEEN B LYMPHOCYTE SURFACE IGD AND FC IGG RECEPTORS THAT DIFFERS FROM THE SURFACE IGM-FC IGG RECEPTOR INTERACTION.

Dickler HB, Kubicek MT, Finkelman FD
Immunology Branch, NCI, NIH, Bethesda, MD, 20205
J Immunol; 128(3):1271-1277 1982

The B lymphocyte surface membrane receptors IgD (sIgD) and Fc IgG receptors (FcgammaR) were evaluated for interactions by means of immunofluorescence. Ligand-(F(ab')2 anti-delta) induced capping of SIgD resulted in co-capping of FcgammaR if the latter were occupied during the capping process by soluble antigen-antibody complexes (which themselves provided insufficient cross-linking to result in capping), but not if the FcgammaR were occupied by monomeric IgG or unoccupied. Capping of FcgammaR by highly cross-linked complexes did not cause co-capping of SIgD occupied by monomeric F(ab') anti-delta. The interaction between sIgD and FcgammaR was specific in that cross-reactions between ligands were excluded and ligand-induced capping of sIgD did not cause co-capping of ligand-occupied sIgM or I-A antigens. The sIgD-FcgammaR interaction occurred on only approx 60% of B lymphocytes, and this B cell subpopulation did not correlate with other B cell subpopulations (CBA/N strain B cells and B cells bearing either large or small amounts of sIgD). The sIgD-FcgammaR interaction differed from the sIgM-FcgammaR interaction in that co -redistribution of the latter two receptors was induced by F(ab')2 anti-mu when the FcgammaR was occupied by monomeric IgG and involved nearly all B lymphocytes. The qualitative and quantitative differences between the sIgD-FcgammaR and sIgM-FcgammaR interactions suggest a mechanism whereby the two antigen receptors could provide different signals to the B lymphocyte. (Author abstract) (54 Refs)

## 51. MEMBRANE ASSOCIATED REGULATORY EVENTS OF LYMPHOID DIFFERENTIATION.

Miller HC, Esselman WJ
Dept. Microbiology and Public Health, Michigan State Univ., East Lansing, MI, 48824
The Handbook of Cancer Immunology: Volume 9- Humoral Immunity in Relation to Cancer. Waters H, ed. New York, Garland STPM Press, 289 pp., 1981.

Purified mouse B-lymphocytes were completely saturated with antigen (Ag), in a way resembling the effect of the absence of T-lymphocytes or of overwhelming microbial, neoplastic, or endogenous Ag assault on the host. Under conditions of Ag saturation, Ag-specific precursor B-cells became tolerant and differentiated no further. The primary B-cells 'overloaded' temporarily (24-48 hr), becoming unable to receive T-cell signals for differentiation into plasma cells. Mitogen or Ag stimulation caused T-cells to shed membrane molecules, including Thy-1 active glycolipids (GL). Modulated B-cells seemed to be only temporarily unable to bind the Ag; they reached full responsive potential by the time T help signals were ready, and thus were protected during the early stages of Ag accumulation. The cells of neuroblastomas and lymphomas (probably other tumor types as well) shed surface GL continuously. This continuous Ag saturation caused B-cells of all specificities to remain in the suppressed, unresponsive stage, which would prevent Ab-mediated host immune reactions and favor tumor growth. Further research is needed to elucidate the regulation of normal immune responses and devise methods of overcoming the deregulation of host defenses by tumor products. (87 Refs)

## 52. MEMBRANE-BOUND AND CELLULAR IMMUNOGLOBULINS IN HUMAN B-LYMPHOMA LINES AND DERIVED HYBRIDS.

Spira G, Aman P, Silvian I, Kolde N, Ber R, Klein G
Faculty Medicine, Technion, P.O.B. 9649, Haifa, 31096, Israel
Immunobiology; 160(3/4):340-351 1981

Hybrids derived from the fusion of cell lines representing different maturation stages were studied for their membrane and cellular immunoglobulin expression. The hybrids can be subdivided into three groups, with one common parental line in each group. In the first group, Raji cells represent the common parent: it contains small amounts of membrane and cytoplasmic mu and kappa chains. In the second group, PUT is the common parent, an ouabain and TG-resistant subline of the BL-derived P3HR-1 line. PUT contains a truncated intracellular mu chain. The third group consists of hybrids between K562, an EBV-negative human e rythroleukemia line and two different BL lines. Membrane-immunoglobulin expression was intermediate between the parental lines in the first two groups derived from the fusion of two BL lines. In the third group, hybridization with the K562 cell suppressed the membrane-Ig expression of the B-cell partner. Total cellular immunoglobulin determinations showed that some cells synthesized light chains in excess of heavy chains, others contained an excess of heavy chains, while still others had equal amounts of heavy and light chains. The hybrids showed a variety of patterns, including amplification of the parental phenotypes, appearance of new phenotypic combinations, and eclipse of one or both parental phenotypes. A comparison of the total and the membrane-associated immunoglobulin patterns suggests independent handling of intracellular and membrane immunoglobulin synthesis. (Author abstract) (28 Refs)

## 53. ACTIVATION OF FC RECEPTOR-BEARING LYMPHOCYTES BY IMMUNE COMPLEXES. I. STIMULATION OF LYMPHOKINE PRODUCTION BY NONADHERENT HUMAN PERIPHERAL BLOOD LYMPHOCYTES.

Neville ME, Lischner HW
Immunology Lab., St. Christopher's Hosp. for Children, Philadelphia, PA, 19133
J Immunol; 128(3):1063-1069 1982

Activation of human peripheral blood lymphocytes by incubation with particulate immune complexes or aggregated human gamma-globulin was studied by measuring the release of leukocyte migration inhibitory factor (LIF) activity. LIF-active supernatants were consistently produced when nonadherent lymphocytes containing less than 1% surface immunoglobulin-bearing cells and less than 0.2% nonspecific esterase-positive monocytes were incubated in the presence of RBC sensitized with rabbit or human antibodies or with pooled heat-aggregated human gamma-globulin. This immune complex-induced lymphokine production (ICLP) was dependent on the presence of cells bearing receptors for the Fc portion of IgG (Fcgamma). ICLP could not be demonstrated with lymphocyte preparations enriched for B cells even though the latter showed vigorous LIF production in the presence of complement-sensitized erythrocytes. ICLP was dependent on the concentration of lymphocytes and of stimulant as well as on the duration of coincubation, and it required active metabolic processes and RNA and protein synthesis but not DNA synthesis. Ca++ but not Mg++ was obligatory. ICLP by non-B Fcgamma receptor-bearing lymphocytes may play a role in antibody-dependent protective inflammation and immunologic

injury phenomena, which is similar to that of lymphokine release by antigen-activated T cells in delayed hypersensitivity responses. (Author abstract) (61 Refs)

## 54. INHIBITION OF HUMAN ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY, CELL-MEDIATED CYTOTOXICITY, AND NATURAL KILLING BY A XENOGENEIC ANTISERUM PREPARED AGAINST 'ACTIVATED' ALLOIMMUNE HUMAN LYMPHOCY TES.

Neville ME, Hiserodt JC
Immunology Lab., St. Christopher's Hosp. for Children, 5th and Lehigh Ave., Philadelphia, PA, 19133
J Immunol; 128(3):1246-1251 1982

Xenogeneic antiserum (RH1) was prepared in Lewis rats by hyperimmunization with concanavalin A- (Con A) activated alloimmune human lymphocytes. The antiserum RH1 effectively inhibited human antibody-dependent cellular cytotoxicity (ADCC), cell-mediated cytotoxicity (CMC), and natural killing (NK) in the absence of complement (C). Inhibition by RH1 was dependent on the dilution of antiserum employed and the number of cytotoxic lymphocytes present during cytolysis. Pretreatment of lymphocytes with RH1 or the presence of RH1 in culture did not inhibit lymphocyte proliferation stimulated by Con A, phytohemagglutinin, or allogeneic cells; lymphokine production as measured by leukocyte-inhibiting factor production; antibody-dependent C lysis; or CMC mediated by murine cytotoxic T lymphocytes. Analysis of the mechanism of inhibition of cytotoxicity by RH1 revealed that (1) RH1 was not cytotoxic for human lymphocytes at 37 C in the absence of C; (2) purified F(ab')2 fragments were equally inhibitory as whole serum; (3) pretreatment of lymphocytes with RH1 effectively inhibited their capacity to mediate ADCC, CMC, or NK, and this effect was reversible by culturing the cells overnight at 37 C; (4) RH1 did not inhibit target cell binding by K cells, effector cells of ADCC, or alloimmune T cells, but did inhibit binding by NK cells; and finally, (5) the addition of RH1 to preformed lymphocyte-target conjugates in a single cell cytotoxicity assay inhibited killing of the bound target cells in all three systems without disrupting the conjugates. Collectively, these findings suggest that RH1 antiserum interacts with structures present on the surfaces of cytotoxic lymphocytes that are involved in the activation of the lytic mechanism(s) or with the actual lytic molecule or molecules themselves. Furthermore, the ability of RH1 to inhibit ADCC, CMC, and NK during the post-binding cytolytic phase of these reactions indicates that binding and cytolysis are distinct and separate events in all types of cell-mediated cytolysis. (Author abstract) (24 Refs)

## 55. DIFFERENTIAL LYSIS OF ENDOGENOUS AND ACTIVATED NATURAL KILLER CELLS BY ANTI-NK-1.2 ANTIBODY AND COMPLEMENT.

Kumar V, Barnes MC, Bennett M, Burton RC
Dept. Pathology, Boston Univ. Sch. Medicine, Boston, MA, 02118
J Immunol; 128(3):1482-1484 1982

Data indicating that natural killer (NK) cells activated by a variety of agents, including lymphocytic choriomeningitis virus, polyinosinic-polycytidilic acid, and interferon, showed markedly diminished expression of the cell surface NK cell-specific alloantigen NK-1.2, to the point where these cells may be totally resistant to lysis by anti-NK-1.2 serum and complement, are presented. ( 15 Refs)

## 56. TWO MONOCLONAL ANTIPLATELET ANTIBODIES AS MARKERS OF HUMAN MEGAKARYOCYTE MATURATION: IMMUNOFLUORESCENT STAINING AND PLATELET PEROXIDASE DETECTION IN MEGAKARYOCYTE COLONIES AND IN IN VIVO CELLS FROM NORMAL AND LEUKEMIC PATIENTS.

Vainchenker W, Deschamps JF, Bastin JM, Guichard J, Titeux M, Breton-Gorius J, McMichael AJ
Hopital Henri Mondor, Unite INSERM U.91, 94010 Creteil, France
Blood; 59(3):514-521 1982

Two monoclonal anti-human platelet antibodies have been used in an immunofluorescent assay to study megakaryocyte maturation. The two antibodies were specific for platelets and megakaryocytes. AN 51 recognizes an antigen on platelet glycoprotein Ib, the antigen detected by J 15 is on the glycoprotein IIb/IIIa complex, since it does not bind to platelets from patients with Glanzmann's thrombasthenia. AN 51 did not stain small cells of normal bone marrow, but it labeled most of the megakaryocytes and all of the platelets. In megakaryocyte colonies, megakaryocytes that had reached full maturity (at day 12 of culture) were stained specifically. AN 51 also labeled micromegakaryocytes (small mature megakaryocytes) in fetal or neonatal cultures and in leukemias, but could not be applied to identification of most leukemia promegakaryoblasts. In contrast, J 15 labeled all megakaryocytes in bone marrow as well as some rare small cells. These cells appear to represent an early cell of the megakaryocyte lineage, since their number was increased in autoimmune thrombocytopenia and they were present as early as the 6th day of culture of megakaryocyte colonies. The size of these cells progressively increased as the culture aged, probably due to endoreplication. In the bone marrow of three patients with leukemias in which promegakaryoblasts were identified ultrastructurally by the presence of platelet peroxidase, J 15 labeled blast cells. Thus, glycoprotein Ib is progressively expressed during megakaryocyte maturation, but its expression is independent of megakaryocyte ploidy, while the glycoprotein IIb/IIIa complex is an early antigenic marker of megakaryocyte maturation that may be useful in isolation of megakaryocyte precursors and diagnosis of megakaryoblastic leukemia. (Author abstract) (32 Refs)

## 57. SURFACE GLYCOPROTEINS OF DIVIDING AND NON-DIVIDING THYMOCYTES.

Salisbury JG
Dept. Biochemistry, St George's Hosp. Medical Sch., London, SW17, ORE, England
Cell Biol Int Rep; 6(2):189-195 1982

The surface glycoproteins labeling of rat large, mainly dividing thymocytes and their small, non-dividing, progeny, by reduction with sodium [3H]borohydride after various oxidative treatments of the cells, is described. Results showed little difference between the two cell types except in the band at 51,000 mol wt, and even after no oxidative pretreatment of the cells a labeled band was obtaine d at 53,000 mol wt with a minor component at 47,000 mo wt. Pretreatment with galactose oxidase induced weak labeling of other proteins including bands at 150,000, 100,000, and 25,000 mol wt. (17 Refs)

## EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS

### 58. IMMUNOREGULATION VIA MODIFIED AMINO GROUPS.

Nehlsen-Cannarella SL
Transplantation Immunology Lab., Montefiore Hosp., Medical Center, Albert Einstein Coll. Medicine, Bronx, NY, 10467
The Handbook of Cancer Immunology: Volume 7- Immune Function and Dysfunction in Relation to Cancer. Waters H, ed. New York, Garland STPM Press, 372 pp., 1981.

The T-lymphocytes are thought to be the primary mechanism of host defense against tumor growth, although many other cells are involved. Sodium cyanate (NaCNO) blocks antigen recognition by (or the activation of) suppressor T-cells, without apparently affecting the memory cells or the 'homing in' of migrating lymphocytes. NaCNO is specific for the T-cell receptor and does not affect the efferent arc of the immune response. NaCNO is directly toxic to a variety of tumors, selectively inhibiting DNA and protein synthesis. The simultaneous administration of deoxycorticosteroid can cancel the immunosuppressive effects of NaCNO on T-cell helper and cytotoxic killer cells. One major goal of tumor immunotherapy is boosting and steering the aberrant immune response to a pathway leading to the destruction of transformed cells. The success of this treatment depends on the initiation of a tumoricidal immune attack which can kill the tumor before suppressive factors or tumor size can inhibit the immune response. NaCNO may be suitable for such immunotherapeutic protocols. (163 Refs)

### 59. ANTIGEN ACTIVATION OF T CELLS.

Lawrence DA
Dept. Microbiology and Immunology, Albany Medical Coll. Union Univ., Neil Hellman Medical Res. Bldg., Albany, NY, 12208
The Handbook of Cancer Immunology: Volume 8- Tumor Antigens: Structure and Function. Waters H, ed. New York, STPM Garland Press, 418 pp., 1981.

Published studies on the biochemical changes which occur in T-lymphocytes after antigen activation have usually failed to make correlations between these biochemical changes and the functional changes expressed by the T-cells, nor have they dealt with the biochemical changes which occur in different subgroups of this heterogeneous population. The first stage in the activation process is the recognition of an immunogenic form of the antigen. Nonspecific macrophage regulation of T-cell activation is apparently a redox function. The suppressor T-cells apparently require more free thiols for the maintenance of their activities than the helper T-cells. The suppressor T-cells are also more dependent on macrophages for their activation than the helper T-cells. The macrophages play a vital role in the maintenance of free sur face thiols, and the suppressor T-cells are more sensitive than the helper T-cells to the loss of surface thiols. A correlation has been found between thiol sensitivity and the radiosensitivity of the suppressor T-cells. As compared to suppressor T-cells, the B-lymphocytes are more sensitive to radiation and sulfhydryl blockage, but their proliferation is less dependent on macrophages. It is suggested that the sensitive thiol-containing components may be on the cell membranes of suppressor T-cells and perhaps intracellular in B-cells. The available evidence suggests that a loss of suppressor T-cells can increase the recurrence of autoimmunity, whereas the loss of cytolytic T-cells leads to the breakdown of immunologic surveillance and an increased tumor incidence. (281 Refs)

### 60. TUMOR PROMOTOR PHORBOL MYRISTIC ACETATE IS A T-CELL-DEPENDENT INDUCER OF IMMUNOGLOBULIN SECRETION IN HUMAN LYMPHOCYTES.

Ralph P, Kishimoto T
Developmental Hemstopoiesis, Memorial Sloan-Kettering Cancer Center, Rye, NY, 10580
Clin Immunol Immunopathol; 22(3):340-348 1982

Human peripheral blood mononuclear cells were induced by 10 to 200 ng/ml phorbol myristic acetate (PMA) to secrete immunoglobulin (Ig). Using protein A-RBC plaque formation to detect secreting cells (PFC), Day 5 and Day 7 PFC induced by PMA were 0.2 to 1.4% of initial numbers of cultured cells. In parallel cultures, pokeweed mitogen (PWM) induced PFC corresponding to 1-3% and 0.6-8% of initial cell numbers, respectively. Suppressor cells for Ig secretion purifying with T (E-rosetting) cells were found in most donors. These were sensitive to mitomycin C. In some donors, PFC responses could only be detected after removal of suppressor cells. By double separation of T cells from B cells, the PMA response was shown to be dependent on T helper cells, similarly to PWM. This is in contrast to a 20-fold stimulation of Ig secretion in some human B culture lines by PMA alone. PMA is thus a T-dependent polyclonal activator for resting, blood B lymphocytes, and a direct stimulator of Ig production in certain dividing lymphoblasts represented by B-cell lines. (Author abstract) (28 Refs)

### 61. EFFECTS OF A TUMOR PROMOTER, 12-O-TETRADECANOYL-PHORBOL-13-ACETATE (TPA) ON HUMAN PERIPHERAL BLOOD LYMPHOCYTES: INDUCTION OF SUPPRESSOR T CELLS AND REDUCTION OF NATURAL KILLING (NK) AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY (ADCC).

Hirata H
Dept. Obstetrics and Gynecology, Mie Univ. Sch. Medicine, Tsu, Japan
Mie Med J; 31(1):37-52 1981

Effects of the tumor promoter, 12-O-tetradecanoyl-phorbol-13-acetate (TPA) were studied in human peripheral blood lymphocytes (PBL) from normal healthy adult donors. Cell suspensions of T cells, B cells, and monocytes were exposed to TPA, concanavalin A (ConA), phytohemagglutinin (PHAP), and pokeweed mitogen (PWM) in various combinations and concentrations. Optimum stimulation of PBL was obtained 96 hr after addition of 10(-7) M TPA. TPA produced significant stimulation of PBL at concentrations of 10(-8)-10(-6) M with peak responses occurring after 3-5 days. TPA nonselectively stimulated T cells and B cells. PHAP and ConA stimulated predominantly T cells. In mixed lymphocyte reactions pretreatment of either the responder T cells or stimulating allogeneic cells with TPA inhibited DNA synthesis. Cells activated by TPA (or supernatant from these cells) suppressed proliferative response by autologous T and B cells to allogeneic cells or mitogens. TPA induced formation of T cells bearing IgG-Fc receptors and T cells forming autologous erythrocyte rosettes. TPA evidently induces suppressor T cells or T cell subsets required for suppressor activity. TPA actively suppressed the activity of natural killer (NK) cells and killer cells effecting antibody-dependent cellular cytotoxicity (ADCC). TPA should be useful for studies of suppressor mechanisms, NK activity, and ADCC. (64 Refs)

## 62. EFFECT OF UREMIC SERUM ON E-ROSETTE FORMATION OF NORMAL LYMPHOCYTES MODULATED BY LEVAMISOLE.

Modai D, Peller S, Weissgarten J, Shaked U, Kaufman S
Dept. Medicine A, Nephrology Unit, Assaf Harofeh Hosp., 61027 Zerifin, Israel
Isr J Med Sci; 17(12):1115-1118 1981

The number of E-rosette forming cells of lymphocytes from healthy subjects was determined under various experimental conditions. Sera from 16 chronic hemodialysis patients were incubated with lymphocytes from 16 matched normal subjects. The effect of levamisole on this combination was studied. Uremic serum markedly inhibited E-rosette formation of normal lymphocytes. Pretreatment with levamisole completely prevented this effect, whereas levamisole treatment following incubation with uremic serum resulted in a partial correction of the E-rosette formation. The hypothesis best fitting these results is that a factor present in uremic serum blocks sheep red cell receptors on normal lymphocytes; levamisole, having a greater affinity for these receptors, prevents or partially corrects the effect of the blockade. (Author abstract) (20 Refs)

## 63. SPONTANEOUS AUTOROSETTE FORMATION IN ACUTE LEUKEMIA PATIENTS.

Mazurenko VA
Hematological Clinic for Adults, Res. Inst. Hematology and Blood Transfusion, Kiev, USSR
Vrach Delo; (7):43-46 1981

Functional activity of T-lymphocytes was studied in 78 patients (17-68 yr old) with acute leukemia (AL). Among these patients, 27 had acute lymphoblastic leukemia, 42 had acute myeloblastic leukemia, and 9 had nondifferentiated variant of AL. Peripheral blood lymphocytes were incubated with autologous RBC, and the number of rosette-forming cells was determined. All AL patients showed marked inhibition of spontaneous rosette-formation. The degree of inhibition did not depend upon the histological variant, stage of AL, or type of therapy. Experiments in Wistar rats showed that administration of 6-mercaptopurine produced significant inhibition of ability of T-lymphocytes to form rosettes with autologous RBC. These findings indicated that chemotherapy can aggravate the functional state of T-lymphocytes in AL patients. (no Refs) (In RUS)

## 64. GLUCOCORTICOID RECEPTOR STUDIES IN HUMAN LEUKEMIA.

Marchetti P, Natoli V, Raneletti FO, Mandelli F, De Rossi G, Iacobelli S
Lab. Molecular Endocrinology, S. Cuore Catholic Univ., 00100 Rome, Italy
J Steroid Biochem; 15:261-268 1981

Glucocorticoid receptors (GR) and glutamine synthetase (GS) activity were measured in leukocytes from peripheral blood of patients with acute lymphoblastic leukemia (ALL). Problems in GR determination, results for GR and response to glucocorticoid treatment and chemotherapy, and presence and inducibility of GS in ALL cells, are discussed. GR density in leukemic lymphoblasts in ALL correlates positively with the short-term response in glucocorticoid treatment and with the inducibility of complete remission, independent of other prognostic factors. (54 Refs)

## 65. GLUCOCORTICOID RECEPTORS AND LEUKEMIA.

Homo F, Duval D, Marie JP, Zittoun R, Harousseau JL
INSERM U7, Hopital Necker, 161, rue de Sevres, F 75015 Paris, France
Ann Endocrinol (Paris); 42(4/5):315-320 1981

Determination of the number of glucocorticoid (GCC) receptors in peripheral cells and the sensitivity of the cells to hormones in vitro and in vivo is described for 27 patients with acute lymphoblastic leukemia. The number of GCC receptors varied from 2,600 to 19,200 sites/cell and showed great variation among the patients. The mean value of 9,000 sites/cell was 2x that of human circulating lymphocytes. The number of receptors has been studied in relation to the metabolic effects of GCC. The relationship among DNA and RNA synthesis, application of GCC, and the number of GCC receptors has been difficult to determine possibly due to the heterogeneity of the populations studied. A relationship has been found between levels of spontaneous incorporation of tritiated uridine and thymidine and the metabolic effects of the steroid. Differences in GCC receptors between circulating WBC and bone marrow cells suggest that examination of circulating cells does not accurately reflect the behavior of the real target cell of GCC therapy. (32 Refs) (In FRE)

## 66. METABOLIC AND ULTRASTRUCTURAL ASPECTS OF THE IN VITRO LYSIS OF CHRONIC LYMPHOCYTIC LEUKEMIA CELLS BY GLUCOCORTICOIDS.

Galili U, Leizerowitz R, Moreb J, Gamliel H, Gurfel D, Polliack A
Dept. Hematology, Hadassah Univ. Hosp., Kiryat Hadassah, P. O. B. 12000, IL-91 120 Jerusalem, Israel
Cancer Res; 42(4):1433-1440 1982

Human chronic lymphocytic leukemia (CLL) cells like prothymocytes and immunoacti vated T-lymphocytes are readily lysed in vitro by pharmacological concentrations of glucocorticoids such as cortisol, whereas peripheral blood lymphocytes and thymocytes are unaffected by the hormone. In this study, metabolic and ultrastructural aspects of the cortisol-induced killing process of CLL cells are recorded. In vitro lysis was found to be temperature dependent and was detected only after 6 to 8 hr incubation with cortisol by means of the trypan blue exclusion test. However, 30 min of incubation with cortisol at either 37 C or 4 C followed by the removal of the hormone was still sufficient to induce the lytic process. Ultrastructural studies demonstrated sequential changes in the cytoplasm, including swelling of mitochondria and cytoplasmic decompartmentalization, followed by loss of surface microvilli with the appearance of 'holes' in the cell membrane, and subsequent condensation of nuclear chromatin. The large holes in the membrane appearing after 6 hr of incubation with the hormone may be the cause for the penetration of the viable stain into the dead cells, as seen by light microscopy. Addition of metabolic inhibitors including actinomycin D, puromycin, and cycloheximide following administration of cortisol resulted in inhibition of the cell lysis. An excess of an antagonist such as cortexolone was found to inhibit the cortisol-induced cytolysis of the CLL cells. It is suggested that the glucocorticoid-induced lysis of human CLL cells is similar to the phenomenon observed in rat or murine lymphocytes and is mediated by interaction of the steroid molecule with the cytoplasmic receptor. The resulting complex appears to activate specific gene(s) the products of which eventually cause cytolysis. (Author abstract) (30 Refs)

### 67. AMYL NITRITE MAY ALTER T LYMPHOCYTES IN HOMOSEXUAL MEN.

Goedert JJ, Wallen WC, Mann DL, Strong DM, Neuland CY, Greene MH, Murray C, Fraumeni JF, Blattner WA

Environmental Epidemiology Branch, NCI, Landow Building - Room 4C18, Bethesda, MD, 20205

Lancet; 1(8269):412-416 1982

To evaluate the recent outbreak of Kaposi's sarcoma (KS) and opportunistic infections in homosexual men, clinical, virological, and immunological data on 2 homosexual men with KS and on 15 healthy homosexual volunteers were collected. Both KS patients had regularly used amyl nitrite or butyl nitrite (AN); they had low helper/suppressor (H/S) T lymphocyte ratios before chemotherapy and high titers of antibody against cytomegalovirus (CMV). Eight of the 15 volunteers were regular AN users; 7 of the 8 had low H/S ratios due to larger than normal numbers of OKT8-positive suppressor cells and smaller numbers of OKT4-positive helper cells. In all eight AN users the fluorescence profile obtained with monoclonal antibody 9.6 (which detects the sheep E-rosette receptor) was bimodal, indicating a subpopulation of T cells with increased receptor density. A similar pattern was observed when OKT8, the antibody which detects cytotoxic suppressor cells, was used. Two of the seven men who did not use AN had abnormal fluorescence with reagent 9.6, and one of these also had a low H/S ratio. CMV-antibody titers were persistently high in 14 of the 15 healthy men, but the titers were not related to An use or T-cell abnormalities. The data suggest that nitrites may be immunosuppressive in the setting of repeated viral antigenic stimulation and may contribute to the high frequency of KS and opportunistic infections in homosexual men. (Author abstract) (35 Refs)

## OTHER RELATED STUDIES

### 68. ANTIBODY MEDIATED DELIVERY OF TOXIC MOLECULES TO ANTIGEN BEARING TARGET CELLS.

Raso V

Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115

Immunol Rev; 62:93-117 1982

The ability of hybrid antibodies with dual specificity to deliver toxic agents to immunoglobulin (Ig)-bearing target cells is reviewed. Progress on both the Ig and CALLA (conjugates which are selectively cytotoxic for human cells bearing the acute lymphoblastic leukemia antigen) are discussed. Topics discussed include hybrid antibodies with simultaneous cell surface and toxic agent binding activity (anti-neocarzinostatin, anti-human IgG hybrids and anti-ricin A chain/anti-human IgG hybrids) and selectively cytotoxic antibody-ricin A chain conjugates (human Ig directed antigen binding fragment [F(ab')]-A chain conjugate, monoclonal human kappa-chain specific F(ab')2-A chain conjugate, and monoclonal CALLA-specific F(ab')-A chain conjugates). Hybrid-mediated enhancement of toxicity has been achieved using neocarzinostatin, whole ricin, and free ricin A chain. (43 Refs)

### 69. THE HANDBOOK OF CANCER IMMUNOLOGY: VOLUME 8: TUMOR ANTIGENS: STRUCTURE AND FUNCTION.

Waters H

NIH, Bethesda, MD

The Handbook of Cancer Immunology: Volume 8: Tumor Antigens: Structure and Function. New York, Garland STPM Press, 418 pp., 1981.

Structural and functional aspects of tumor antigens are reviewed. Mechanisms of reactions between lymphocytes and antigens are discussed. Characteristics of Ia antigens in mice and humans are presented and the significance of these antigens is considered. Histocompatibility antigens and tumor-associated antigens in plasma and urine are discussed and their diagnostic significance evaluated. Molecular structure and mechanisms of antibody-antigen interactions are outlined. Other topics include the use of cell membranes to assess phenotypic expression, masking of cancer-cell surface antigens, cell surface modulation in mammary cancer, antigen activation of T cells, assay and structure of carcinoembryonic antigens, induction of immune response to tumors induced by simian virus 40, and tumor-associated immunosuppressive serum proteins. Concentration and distribution of antigens are related to normal and pathological conditions. Discussion includes review of literature, presentation of original findings, and speculation on future research efforts. Converging and diverging viewpoints are expressed. (1659 Refs)

### 70. BENCE JONES PROTEINS: MALIGNANT OR BENIGN?

Solomon A

Center Health Sciences, Knoxville Unit, Coll. Medicine, Univ. Tennessee, Knoxville, TN, 37920

N Engl J Med; 306(10):605-607 1982

Whether benign monoclonal gammopathies are truly benign or presage the eventual development of a plasma-cell/lymphocytic neoplasm or amyloidosis is discussed. The transition from benign to malignant gammopathy has been reported in patients with monoclonal serum immunoglobulins. At least 60-80% of patients with multiple myeloma have Bence Jones proteinuria; in approx 20% of patients, Bence Jones proteins (BJP) may be the sole monoclonal immunoglobulin formed by the malignant plasma cell. Response or lack of response to chemotherapy can be documented by measurement of daily excretion of BJP. Appearance of BJ proteinuria in patients with myeloma usually signifies a transition to a more aggressive form of disease. BJP themselves are probably malignant entities with pathophysiologic effects, the most important of which are those on the kidney. Renal dysfunction in patients with BJ proteinuria may appear as proximal or distal tubular effects, nephrotic syndrome, or the development of azotemia. BJP are indicators of the primary or myeloma-associated form of amyloidosis. A poorer prognosis is associated with patients with lambda type of BJP than those with kappa type. Chemotherapy is recommended for symptomatic myeloma patients with BJP in their plasma or urine. Caution should be exercised for asymptomatic patients with BJP because of the toxicity and potential mutagenic of the drugs used. (15 Refs)

## 71. RADIOIMMUNOMETRIC DEMONSTRATION OF IMMUNOGLOBULIN G ON CANCER CELLS DERIVED FROM MALIGNANT PLEURAL EFFUSIONS.

Gorny MK, Micksche M, Wolf A
Inst. Biostructure, Poznan, Poland
Oncology; 39(1):6-12 1982

Well-preserved viable cancer cells, lymphocytes and mesothelial cells were prepared from various human malignant and non-malignant pleural effusions by a Ficoll-Hypaque discontinuous gradient. Using 125I-labeled protein A from Staphylococcus aureus as tracer, IgG was found on all cancer cells and also on apparently non-malignant mesothelial cells. Loss of cell surface IgG by overnight incubation, and fluctuation of surface IgG levels in the same patient occurred with cancer cells as well as with mesothelial cells. The IgG in vivo coat of cancer cells reflected the IgG levels of the sera rather than those of the pleural effusions. Binding of IgG from autologous and allogeneic sera and from supernatants of acid and mil d overnight elution of cancer cells and mesothelial cells did not indicate a cancer-specific uptake of IgG. Various unspecific modes of IgG uptake by cancer cells are discussed including the possibility of a non-immune mechanism. Modification and loss of antigens by metastatic cells have also been considered. (Author abstract) (30 Refs)

## 72. 'HIDDEN' CYTOTOXIC ANTIBODIES THAT REACT WITH ALLOGENEIC CULTURED FETAL AND TUMOR CELLS CONTAINED IN SOLUBLE IMMUNE COMPLEXES FROM NORMAL HUMAN SERA.

Morgan AC, Rossen RD, McCormick KJ, Stehlin JS, Giovanella BC (c/o Rossen) Immunology Res. Lab., Veterans Admin. Medical Center, Building 211, Room 203, 2002 Holcombe Blvd., Houston, TX, 77211
Cancer Res; 42(3):881-887 1982

Hidden complement-dependent cytotoxins were demonstrated in normal donor sera after removing anti-immunoglobulins that normally block the ability of these immunoglobulin Gs to react with surface antigens on tumor cells. The blocking antibodies had certain properties of anti-idiotypes. Immunoglobulin G from Cohn Fraction II, after removing these anti-immunoglobulins, was cytotoxic for cultured fetal cells and for malignant melanoma, breast, lung, colon, and other tumor cells maintained either in tissue culture or by serial passage in nude mice. The cytotoxins were not adsorbed by extracts from normal lymphoid, liver, skin, or red blood cells. These results suggest that a heterogeneous group of natural antibodies reactive with antigens expressed on a variety of neoplastic and fetal cells circulate in normal donor sera as part of a soluble immune complex, together with a blocking anti-immunoglobulin. (Author abstract) (39 Refs)

## 73. PRELIMINARY STUDIES ON ESTIMATION AND APPLICATION OF LYMPHOCYTE ALPHA-NAPHTHYL ACETATE ESTERASE.

Sun G, Liao Y, Zhu X, Zhou S, Xue Z, Li G, Dai Y, Hu Y, Zheng S
Dept. Biochemistry, Pediatric Inst., Chinese Acad. Medical Sciences, Beijing, People's Republic of China
Zhonghua Yixue Jianyan Zazhi; 4(2):76-78 1981

Alpha-naphthyl acetate esterase (ANAE) activity is generally considered a characteristic of T-lymphocytes. This study was undertaken to evaluate the conditions for the ANAE assay, factors that influence its accuracy and the relationship between ANAE activity and T-lymphocytes. Results indicated that although most T-lymphocytes had ANAE activity, this activity was not unique to the T-cells, especially in pathological conditions such as leukemia. Furthermore, substrate concentration, pH and reaction time also influenced the assay results. (4 Refs) (In CHI)

## 74. PRODUCTION OF LEUKOCYTE MIGRATION INHIBITION FACTOR BY LYMPHOCYTES OF LARYNX CANCER PATIENTS STIMULATED BY LARYNGEAL CARCINOMA SOLUBILIZED MEMBRANE ANTIGENS.

Cortesina G, Cavallo GP, Beatrice F, Sartoris A, Bussi M, Morra B, Di Fortunato V, Poggio E, Rendine S
II Clinica Otorinolaringologica, Universita di Torino, Via Genova 3, 10126 Torino, Italy
Tumori; 68(1):39-46 1982

The production of leukocyte migration inhibition factor (LIF) from lymphocytes after stimulation with 3 M KCl soluble tumor and normal mucosa extracts was investigated in 30 patients with laryngeal carcinoma at different developmental stages and in 30 normal donors. The experiments were performed in heterologous and autologous systems. In heterologous systems 3 M KCl tumor extracts induced LIF production by heterologous lymphocytes from patients in 91% of the cases, and normal mucosa extracts induced LIF production by heterologous lymphocytes from patients in 73% of the cases and from normal donors in 90% of the cases. In autologous systems 3 M KCl tumor extracts induced LIF production by autologous lymphocytes from the same patients in 65% of the cases, whereas the normal laryngeal mucosa extracts induced LIF production by the same autologous lymphocytes in 6% of the cases. The high positivity percentage of the test in heterologous systems could be related to differences in the major histocompatibility complex. The 65% test positivity in autologous systems using tumor extracts could be related to the presence of tumor associated antigens. (Author abstract) (20 Refs)

## 75. HUMAN HELPER T CELL FACTOR(S) (THF). II. INDUCTION OF IGG PRODUCTION IN B LYMPHOBLASTOID CELL LINES AND IDENTIFICATION OF T CELL-REPLACING FACTOR-(TRF)LIKE FACTOR(S).

Teranishi T, Hirano T, Arima N, Onoue K
Dept. Immunobiochemistry, Kumamoto Univ. Sch. Medicine, 2-2-1, Honjo, Kumamoto 860, Japan
J Immunol; 128(4):1903-1908 1982

IgG-PFC was induced in Epstein-Barr virus-transformed B lymphoblastoid cell lines (LCL) by the addition of allogeneic T cells. T cells involved in the induction of IgG-PFC were shown to belong to the Leu 3a+/2a- T cell subset. Furthermore, partially purified soluble factors obtained from the culture supernatant of PPD-stimulated pleural T cells or PWM stimulated tonsillar mononuclear cells was shown to induce IgG-PFC in LCL across the major histocompatibility complex barrier. The induction of IgG-PFC was observed only in surface IgG-positive LCL cell populations and was not accompanied by the increase in the number of LCL cells. The factors with such a TRF-like activity were found in two fractions corresponding to the mol wt range of 18,000 to 25,000 (22K fraction) and 28,000 to 38,000 (36K fraction) by gel filtration. Isoelectric focusing at these fractions revealed that TRF-like activity of both 22K and 36K fractions distributed in the pI range of 5.0 to 6.0, and both fractions were found to be devoid of TCGF activity. These results appear to indicate that the factors act on the B cells in terminal stages to trigger final differentiation to Ig-producing cells. (Author abstract) (35 Refs)

## 76. THE INVOLVEMENT OF TWO DISTINCT SUBSETS OF T CELLS FOR THE EXPRESSION OF THE IGE CLASS-SPECIFIC SUPPRESSION: ESTABLISHMENT AND CHARACTERIZATION OF PC-SPECIFIC, T15 IDIOTYPE-POSITIVE T HYBRIDOMAS AND IGE CLASS-SPECIFIC, ANTIGEN-NONSPECIFIC T HYBRIDOMAS.

Sugimura K, Nakanishi K, Maeda K, Kashiwamura SI, Suemura M, Shibo O, Yamamura Y, Kishimoto T

Third Dept. Medicine, Osaka Univ. Medical Sch., Fukushima-ku, Osaka 553, Japan

J Immunol; 128(4):1637-1644 1982

PC-Myc-primed T cells showed PC-specific suppressor function selectively on the IgE antibody response. Treatment of PC-Myc-primed T cells with anti-T15 idiotypic antibody and complement abolished the IgE class-specific suppressor function and the suppressor effect of PC-Myc-primed T cells could be enriched by employing anti-T15 idiotypic antibody-coated petri dishes, showing the involvement of T15 idiotype-positive T cells in the IgE class-specific suppression. Somatic cell hybridization of PC-Myc-primed T cells with BW5147 could give rise to two distinct types of hybridomas, ie, PC-specific and IgE class-specific. PC-specific hybridomas were stained with anti-T15 idiotypic antibody and showed rosette formation with PC-SRBC, which was inhibited by the addition of anti-T15 idiotypic antibody. The culture supernatant obtained from these hybridomas showed a PC-specific suppressor effect on the IgE, as well as IgG, responses. PC-binding molecules could be isolated from the surface-labeled PC-specific hybridomas by affinity chromatography and their mw was approx 64,000 by SDS-PAGE analysis. On the other hand, IgE class-specific hybridomas did not express any PC-binding molecules when tested by immunofluorescence or the rosette formation. No PC-binding molecules could be isolated from these cells by employing the same conditions applied to PC-specific hybridomas. The culture supernatant showed the antigen-nonspecific suppressor function selectively on the IgE response. When taken collectively, these results suggest the involvement of two distinct subsets of T cells for the expression of the IgE class-specific suppression. (Author abstract) (37 Refs)

## 77. NATURAL KILLER (NK) CELLS AND THEIR POSSIBLE ROLES IN RESISTANCE AGAINST DISEASE.

Herberman RB

Lab. Immunodiagnosis, NCI, Bethesda, MD, 20205

Clin Immunol Rev; 1(1):1-65 1981

The characteristics of natural killer (NK) cells and their relation to host resistance to disease are reviewed. Topics discussed include the following: general phenotype of NK cells; expression of markers restricted to NK cells; cell lineage of NK cells; possible relationship of NK cells to T cells, macrophages, or monocytes; interpretation of available evidence regarding lineage of NK cells; possible in vivo roles of NK cells; role of NK cells in resistance against tumor cell lines, primary tumor s, microbial infections, and bone marrow transplants; role of NK cells in graft-vs-host disease and in regulation of differentiation of normal hematopoietic or other cells; NK cells as secretory and immunoregulatory cells; clinical correlations of NK cells; and implications of NK cells for immunotherapy. (279 Refs)

## 78. STUDIES ON NATURAL KILLER (NK) CELLS. III. THE EFFECTS OF IN VITRO CULTURE ON SPONTANEOUS CYTOTOXICITY OF MURINE SPLEEN CELLS.

Bartlett SP, Burton RC

Transplantation Unit, Harvard Medical Sch. at Massachusetts General Hosp., Boston, MA, 02114

J Immunol; 128(3):1070-1075 1982

In vitro culture of normal lymphohemopoietic cells is a complex event leading to the generation of a diverse group of effector cells. When murine spleen cells are cultured by themselves in fetal calf serum containing medium for up to 9 days, at least three distinct subpopulations of cytotoxic effectors can be distinguished on the basis of tumor target cell preference and expression of cell surface alloantigens. Fresh spleen cell suspensions contain two distinct NK cell types: NK-1.2+ NKA cells, which preferentially lyse lymphoma targets, and NK-1.2-NKB cells, which lyse nonlymphoma, mainly solid tumor targets. These NK cells account for all the cytolytic activity on day 0 of culture. NK-1.2+ NKA cells are very labile, and greater than or equal to 80% of their activity is lost within 48 hr of culture. By contrast, the activity of NKB cells increases in culture, up to four-fold by day 6, and solid tumor target cells resistant to lysis by fresh spleen cells now become susceptible. In addition, an NK-1.2-, H-2+, Thy-1.2+, Ly-1.2+, Ly-2.2+ cytotoxic effector cell arises in culture from, or is dependent upon the presence of, NK-1.2-, Thy-1.2+ cells. This spontaneously arising 'Tc' has a peak of activity between day 3 and 6 of culture, and kills a variety of lymphohemopoietic tumor cell types. (Author abstract) (35 Refs)

## 79. TWO DISTINCT HUMAN CLONED T CELL LINES THAT EXHIBIT NATURAL KILLER-LIKE AND ANTI-HUMAN EFFECTOR ACTIVITIES.

Sugamura K, Tanaka Y, Hinuma Y

Inst. Virus Res., Kyoto Univ., Sakyo-ku, Kyoto 606, Japan

J Immunol; 128(4):1749-1752 1982

Cloned T cell lines from mixed lymphocyte cultures stimulated with autologous Epstein Barr virus- (EBV) transformed lymphoblastoid cell line (LCL) cells were established using a limiting dilution technique in the presence of T cell growth factor (TCGF). The T cell lines included two distinct clones of cytotoxicity T cells (Tc) in addition to EBV-specific Tc. A cytotoxic profile of one cloned line was similar to that of endogenous NK cells in peripheral blood. The other cloned Tc line showed an anti-human cytotoxicity. The susceptible targets for this latter Tc line were various human cells, including autologous LCL and peripheral blood lymphocytes (PBL), stimulated with pokeweed mitogen, along with NK-sensitive and NK-resistant cell lines. Weak cytotoxic activity was detected against various xenogeneic cell lines. Furthermore, autologous and allogeneic cloned T cell lines were resistant to killing by the anti-human effector clone. These two distinct cloned Tc lines expressed the Leu-1 and Leu-2a antigens, which are markers of suppressor/cytotoxic T cells. (Author abstract) (23 Refs)

## 80. LONG-TERM CULTURE, CLONING, AND SURFACE MARKERS OF MIXED LEUKOCYTE CULTURE-DERIVED HUMAN T LYMPHOCYTES WITH NATURAL KILLER-LIKE CYTOTOXICITY.

**Pawelec GP, Hadam MR, Ziegler A, Lohmeyer J, Rehbein A, Kumbier I, Wernet P**
**Immunology Lab., Medizinische Klinik, 7400 Tubingen, W. Germany**
**J Immunol; 128(4):1892-1896 1982**

Human lymphocytes alloactivated in mixed leukocyte cultures (MLC) can exert specific cell-mediated cytotoxicity against normal allogeneic targets and against certain cell lines. The former is directed by defined alloantigens expressed by almost all normal tissues, the latter against as yet undefined structures expressed predominantly by transformed tumor and virus-infected cells. This type of alloantigen-unrestricted cytotoxicity may be considered analogous to the spontaneous cytotoxicity mediated by unprimed, freshly isolated normal lymphocytes designed 'natural killing' (NK). The NK-like cytotoxic cells recovered from MLC are shown here to be susceptible to the growth-promoting properties of interleukin 2 (IL 2) containing culture supernatants of phytohemagglutinin-stimulated leukocytes. The NK-like cytotoxic patterns are retained for the finite (65 to greater than 80 days) life spans of these IL 2-dependent cell lines. From these, clones can be isolated by limiting dilution, which manifest exclusively NK-like or alloantigen-directed cytotoxicity. The cloned cells also retain cytotoxic activity up to the end of their life spans. Surface marker phenotyping of selected clones shows that they are mature activated T cells (OKT3+, Lyt-3+, UCHT1+, HLA-DR+, HTA1-). Cloned cells can possess either of the mutually exclusive OKT4+/OKT8-or OKT4-/OKT8+ phenotypes, but with no relation to cytotoxic or helper functions. Two monoclonal antibodies, OKM1 and M522, which are known to deplete almost all NK activity from freshly prepared peripheral blood mononuclear cells, react differently on cloned cells. M522 is expressed only by clones with cytotoxic function (NK-like or alloantigen-directed), whereas OKM1 is expressed only weakly on NK-like clones. In contrast, expression of structures detected by the rat monoclonal antibody YD1/48.HLK is restricted exclusively to those clones with NK-like function. The results presented here indicate that human NK-like phenomena are amenable to analysis at the clonal level by using IL 2-driven cell lines. (Author abstract) (34 Refs)

## 81. CELLS BEARING FC RECEPTORS IN HUMAN MALIGNANT SOLID TUMOURS.

**Svennevig JL, Andersson TR**
**Dept. Surgery, Rikshospitalet, Oslo, Norway**
**Br J Cancer; 45(2):201-208 1982**

Fc-receptor-bearing cells forming EA rosettes with antibody-coated human erythrocytes (Ripley) were studied in cell suspensions and in purified preparations of mononuclear cells (MC) from 20 human malignant tumors. The EA rosettes were studied in preparations made by cytocentrifugation and the rosette-forming cells identified by their nonspecific-esterase activity and phagocytic capacity. Fc receptors were found on 16 +-20% of all cells in the primary cell suspensions. Significantly more tumor-infiltrating lymphocytes had detectable Fc receptors (33 +-18%) than did peripheral-blood lymphocytes in cancer patients (19 +-8%) and normal control subjects (14 +-6%). There was a significant correlation between the proportion of lymphocytes lacking T and B markers (null cells) and the proportion of lymphocytes with Fc receptors. Fc receptors were also found on most tumor-infiltrating macrophages, on some T lymphocytes and polymorphonuclear cells and on a smaller percentage of the tumor cells. The significance of the Fc receptor and its usefulness as a marker of 'host infiltration' into the tumors is discussed. (Author abstract) (29 Refs)

## 82. DISCRIMINATION ANALYSIS IN THE CHOICE OF APPROPRIATE IMMUNOLOGICAL TEST METHODS IN PATIENTS WITH BRONCHIAL CARCINOMA.

**Janatkova I, Havranek T, Prochazka J, Kugukovova Z, Sobeslavsky C**
**Oddeleni tuberkulozy a respiracnich nemoci, Ustredni vojenske nemocnice, Bulovka, 180 71 Prague 8, Czechoslovakia**
**Stud Pneumol Phtiseol Cech; 41(10):682-687 1981**

The results of immunological diagnostic tests performed in 86 men with confirmed bronchial carcinomas and in 30 blood donors (all men) were subjected to discrimination analysis to identify the most suitable combination of methods for the distinction of the patients from the healthy subjects. The diagnostic tests included leukocyte count, percentage of lymphocytes in the peripheral blood, blast transformation of lymphocytes after activation with phytohemagglutinin, percentage of active lymphocytes, nucleolar coefficient, IgG, IgA, and IgM levels, and E-rosette test. The combination of blast transformation and E-rosette test was found to be best suited for the diagnosis of lung cancer, because it permitted 99.1% of the lung cancer patients to be identified and distinguished from the blood donors. (17 Refs) (In CZE)

## 83. CLINICAL ASSESSMENT OF PATIENTS WITH HEAD AND NECK CANCERS USING HEMATOLOGICAL, SEROLOGICAL, AND IMMUNOLOGICAL PARAMETERS.

**Okamoto M**
**Dept. Otorhinolaryngology, Kitasato Univ. Sch. Medicine, Kanagawa 228, Japan**
**Nippon Jibiinkoka Gakkai Kaiho; 84(11):1408-1423 1981**

Hematological, serological, and immunological parameters were assessed in 121 patients (92 men, 29 women) who had squamous cell carcinoma of the head and neck region and who were treated with either surgery or radiotherapy. Sites of cancers included the upper jaw in 29 of the patients, larynx in 45, upper pharynx in 18, middle pharynx in 5, cheek in 4, and others in 20. Peripheral blood lymphocyte count, T-cell count, and phytohemagglutinin blast-formation rate were used as parameters of cellular immunity. Serum immunoglobulins, complement components C3 and C4, CH50, carcinoembryonic antigen, and alpha-1-antitrypsin were used as parameters of humoral factors. Prior to treatment, the patients with pharyngeal cancer, advanced cancer, or poor prognosis frequently showed subnormal cellular immunity. Decreases in markers of cellular immunity varied according to treatment; marked decreases following treatment were observed particularly in patients with pharyngeal, upper jaw, or advanced cancer. The decreased cellular immunity following treatment improved rapidly after surgery but more slowly after radiotherapy. Hematological, serological, and immunological parameters must be considered along with appearance and functional preservation when treatment is being chosen for patients with head and neck cancers. (42 Refs) (In JPN)

## 84. IMMUNOLOGIC STATE OF PATIENTS WITH OPERABLE MAMMARY CANCER.

Hrsak KM, Rudnif M, Kubovic M, Marticac P, Bulic N, Katelan M
Zavod za klinicku onkologiju i radioterapiju, Klinicki bolnicki centar, Rebro, Zagreb, Yugoslavia
Libri Oncol; 10(2/3):323-326 1981

Immunologic state was evaluated in 44 healthy controls (HC) and in 49 patients with operable mammary cancer (MC) in different stages of the disease with the aid of mitogens reactivity [phytohemagglutinin (PHA), concanavalin A (Con A), and pokeweed mitogen (PWM)], T and B lymphocytes, and the most active T lymphocytes (E, M, and A rosettes) in peripheral blood. Patients were tested before receiving any therapy. Reactivity to mitogens was lower in MC compared with HC patients. Most pronounced reactivity was seen when tested with PHA. Difference in reactivity between Stage I and the other two could be observed. Total number of T and B lymphocytes was reduced, but that reduction was less significant than the reactivity to mitogens. Most active T lymphocytes were higher in Stage II patients with MC than in HC. (8 Refs) (In SCR)

## 85. DEPLETION OF LYMPHOCYTE SUBPOPULATIONS IN PRIMARY AND SECONDARY LYMPHOID ORGANS OF MICE BY A TRANSPLANTED GRANULOCYTOSIS-INDUCING MAMMARY CARCINOMA.

Lee MY, Rosse C
Div. Hematology, Dept. Medicine RM-10, Univ. Washington Sch. Medicine, Seattle, WA, 98195
Cancer Res; 42(4):1255-1260 1982

Transplanted CE mammary carcinoma causes a marked increase in the production of neutrophilic granulocytes in mice associated with the expansion of hemopoietic marrow into the peripheral ske leton. Changes in lymphocyte populations in the femoral marrow, the expanding peripheral marrow, and the spleen were examined for a period of 3 wk post-tumor transplantation using fluoresceinated antisera specific for B- and T-cells. As tumor growth and granulocytic hyperplasia progressed, B- and T-cells became reduced in femoral marrow and the spleen, but lymphocytes of undefined function, devoid of T- and B-cell surface antigens (null cells), transiently increased in femoral marrow and in the spleen. In the expanding peripheral marrow, such null cells increased and remained as the predominant cell type until granulocytic hyperplasia took place. These changes suggest shifts in the site of myelogenous lymphocyte production or in the differentiation program of lymphocytes. The thymus invariably showed marked atrophy which, as shown in adrenalectomized animals, could not be explained entirely by tumor-induced stress. Thus, the massive granulocytopoietic effects of CE mammary carcinoma are coupled with marked changes in lymphocyte populations due, most likely, to the tumor's influence on primary lymphoid organs. (Author abstract) (26 Refs)

## 86. IMMUNE REACTIVITY IN COLORECTAL CARCINOMA: CLINICAL VALUE FROM A SURGICAL VIEWPOINT.

Muhrer KH, Schwemmle K, Filler D, Kahle M
Chirurgische Universitatsklinik, Klinikstrasse 29, D-6300 Giessen, W. Germany
Chirurg; 53(2):112-116 1982

Specific immune reactions to colorectal carcinoma (CRC) were studied. NaCl extracts of tumor cell-membrane proteins were made from samples of CRC, gastric cancer (GC), bronchial carcinoma (BC), and mammary carcinoma (MC). CRC types included well, moderately, and poorly differentiated adenocarcinoma. Lymphocytes preparations were made from venous blood of 36 patients with histologically confirmed CRC, 15 patients with precancerous adenoma of the colon, 19 patients with inflammation of the colon, and 54 healthy controls. Reactivity to tumor antigens was measured by inhibition of electrophoretic cell migration using sheep RBC as indicator cells. Inhibition of greater than 5% was considered positive. Positive reactions to CRC extract were obtained with lymphocytes from 31/36 CRC patients. Average inhibition was 12.0 +-7.03% for Duke's Stage A CRC, 11.18 +-5.06% for Stage B, 13.26 +-7.03% for Stage C, and 16.80 +-7.65 % for patients with extensive metastases. Negative results were obtained from 48/56 controls. Positive results were obtained from 10/15 patients with adenoma and 11/19 patients with inflammatory conditions. Of 36 CRC patients, 8 showed positive reactions to GC extracts; none showed positive reactions to BC or MC. Reactivity to allogeneic tumor extracts indicated the sensitivity was specific for the tumor type rather than for the individual. Results indicate specific sensitivity of lymphocytes from CRC patients to CRC antigens and some weak cross -reactivity to antigens from other tumor types. Reliability of the test is limited by positive sensitivity of patients with acute inflammatory conditions. (15 Refs) (In GER)

## 87. IMMUNOPATHOLOGY OF CANCER OF THE LEFT COLON AND RECTUM. EVALUATION OF SOME PARAMETERS RELATED TO IMMUNOLOGIC RESPONSE OF THE HOST.

Naves A, Pollastri E, Dip O, Mancuso O, Puig N, Bravo Luna M, Amerio N, Morini JC
Centro de Onsologia, Hospital N del Centenerio, Rosario, Argentina
Rev Fac Cienc Med Univ Nac Rosario; 14(2):19-22 1981

Thirty patients (both sexes, 36-76 yr old) with cancer of left colon and rectum were treated by colectomy or coloproctectomy. Sections of original tumors, sections of tumors proximal and distal, and regional lymphatic ganglions (RLG) were examined. Staging according to TNM (tumor, lymph node, metastasis) indicated that 24 of the patients had neoplastic invasion reaching adipose tissue beyond muscle tissue and that 12 of the 24 had metastases in the RLG. Indexes of malignity of the tumors (IMT) were calculated, based on tumoral invasion, cortical and paracortical hyperplasia, local immune response (mononuclear cells in the border of the tumoral invasion), and perivascular lymphocytosis. Also at the time of diagnosis, peripheral blood was removed and concentrations of E rosettes were determined. The IMT was lower in patients who had curative surgery and was negatively correlated with age and with the concentration of E rosettes. It was concluded that local and general immunity of the host should be evaluated for better understanding of the physiopathology and evolution of the neoplastic process. (5 Refs) (In SPA)

## 88. LYMPH NODE T CELLS IN HODGKIN'S DISEASE: ANALYSIS OF SUSPENSIONS WITH MONOCLONAL ANTIBODY AND ROSETTING TECHNIQUES.

Aisenberg AC, Wilkes BM
Huntington Lab., Massachusetts General Hosp., Boston, MA, 02114
Blood; 59(3):522-527 1982

Suspensions prepared from lymph nodes involved by Hodgkin's disease and from a diverse group of lymph node hyperplasias were investigated with a panel of 10 monoclonal antibodies and a variety of conventional surface marker tech-

niques. In both Hodgkin's disease and hyperplasia, 60%-70% of the cells were T lymphocytes, approximately 80% of the inducer/helper subset and 20% of the cytotoxic/suppressor subset. The most prominent differences observed between Hodgkin's disease and hyperplastic T cells are explained by greater affinity of the sheep cell receptor on the surface of the lymphoma T lymphocytes. This greater affinity was best demonstrated by the formation of rosettes with unsensitized or immunoglobulin-sensitized sheep erythrocytes after incubation at 37 C, an occurrence observed only with Hodgkin's disease cells. In addition, in hyperplasia, a variable proportion of lymphocytes reacting with the anti-T-cell monoclonal antiserum OKT3 failed to form unsensitized rosettes at 4 C (E rosettes), while in Hodgkin's disease there was near equivalence of T cells that reacted with the antiserum and formed E rosettes. In addition to the increased infinity for sheep erythrocytes, some Hodgkin's disease specimens displayed increased reactivity with the monoclonal antibody OKM1, which detects monocytes and granulocytes, and the monoclonal antibody OKT10, which reacts with early thymocytes. Finally, 14 of 20 lymphoma samples exhibited polar migration of the fluorescent material (capping) with one or more antisera (most frequently OKI1, the monoclonal antibody with specificity for the Ia-like antigen). These findings are useful in distinguishing Hodgkin's disease lymph nodes from hyperplasia by surface marker characteristics and may be relevant to older observations that Hodgkin's disease T cells aggregate about Reed-Sternberg cells. (Author abstract) (26 Refs)

* U. S. GOVERNMENT PRINTING OFFICE : 1982—361-347/123

# AUTHOR INDEX WITH CITATION NUMBERS


Aisenberg AC 88
Aliberti A 25
Aman P 52
Amerio N 87
Andersson TR 81
Antonelli G 25
Arima N 75
Astaldi G 21
Auchincloss H 36
August JT 47
Babusikova O 26
Barnes MC 55
Bartlett SP 78
Bastin JM 56
Beatrice F 74
Belardelli F 25
Beller DI 48
Bellouard A 5
Bennett M 55
Ber R 52
Bergman Y 32
Bernard A 10
Bernard J 42
Bernstein ID 35
Blackstock R 1
Blattner WA 12
Blattner WA 67
Bollum FJ 45
Bom-Van Noorloo 9
Borst J 34
Bottero L 18
Boumsell L 10
Bourikas G 12
Bowman WP 10
Braun C 22
Braun J 20
Bravo Luna M 87
Breton-Gorius J 56
Bricker MD 23
Bridges JM 12
Brownell AI 12
Bulic N 84
Burton RC 55
Burton RC 78
Bussi M 74
Cailla H 7
Cailla HL 4
Caillaud J 10
Calama' EG 48
Carcassonne Y 4
Carcassonne Y 7
Catovsky D 12
Catovsky D 6
Cavallo GP 74
Chardonnens X 37
Chorvath B 26
Cleton FJ 9
Cooper SM 23
Cordier G 24
Cortesina G 74
Cramer A 13
D'Agnolo G 25
Dai Y 73
De Heer E 16
De Rosai G 64
De Weger RA 16
Den Otter W 16
Deschamps JF 56
Di Fortunato V 74
Dibar E 2
Dickler HB 50
Diez RA 5
Dip O 87
Dishkant IP 39
Divito J 2
Dullens HF 16
Duraj J 26
Duval D 65
Eichmann K 28
Esselman WJ 51
Estevez ME 2
Estevez ME 5
Filler D 86
Finiasz MR 2
Finkelman FD 50
Fontaine M 22
Fraumeni JF 67
Froment Y 37
Galili U 66
Gallo RC 12
Galton DA 12
Gamliel H 66
Gastaut JA 4
Gastaut JA 7
Gilbert K 49
Giovanella BC 72
Giraudo Conessa 21
Giuntoli J 2
Goedert JJ 67
Goldman JM 6
Goldstein G 27
Golstein P 33
Goolden AW 12
Goridis C 33
Gorny MK 71
Goto Y 46
Goujet-Zalc C 22
Greaves MF 12
Greaves MF 27
Greaves MF 29
Greene MH 67
Guichard J 56
Gurfel D 66
Hadam MR 80
Hammerling GJ 28
Harlozinska A 8
Harousseau JL 65
Havranek T 82
Herberman RB 77
Hilgers J 16
Hinuma Y 79
Hirano T 75
Hirata H 61
Hiserodt JC 54
Ho MK 43
Hochman PS 20
Hoffmann MK 49
Homo F 65
Hrsak KM 84
Hu Y 73
Humphrey GB 1
Hyman R 40
Iacobelli S 64
Ido M 3
Ignat'eva GA 39
Ireland R 12
Jakobiec FA 15
Janatkova I 82
Janossy G 27
Jeannet M 37
Johnson HM 38
Joye MT 37
Kahle M 86
Kashiwamura SI 76
Katelan M 84
Kaufman S 62
Kersey JH 29
Kersey JH 45
Kishimoto T 60
Kishimoto T 76
Klein G 19
Klein G 52
Knowles DM 15
Kobayashi Y 46
Koide N 52
Konno T 46
Koubek K 27
Kubicek MT 50
Kubovic M 84
Kugukovova Z 82
Kumar V 55
Kumbier I 80
Kung P 27
Lampert I 12
Lane BC 23
Lange B 18
Lawinska B 8
Lawrence DA 59
LeBien TW 45
Lebien TW 29
Lebman D 18
Lee MY 85
Leizerowitz R 66
Lemerle J 10
Lesley J 40
Lesley J 41
Levy R 32
Li G 73
Liao Y 73
Lischner HW 53
Lohmann-Matthes 44
Lohmeyer J 80
Lopez F 17
Lukes RJ 13
Maeda K 76
Mahouy G 22
Man'ko VM 39
Mancuso O 87

Mandelli F. 64
Mann DL. 67
Maraninchi D. 4
Maraninchi D. 7
Marchetti P. 64
Marie JP. 65
Martinac P. 84
Maurer R. 13
Mazurenko VA. 63
McCluskey DR. 12
McCormick KJ. 72
McKenzie IF. 30
McMichael AJ. 56
Melief CJ. 6
Melief CJ. 9
Melvin S. 10
Micksche M. 71
Miller HC. 51
Modai D. 62
Moreb J. 66
Morgan AC. 72
Morini JC. 87
Morra B. 74
Muhrer KH. 86
Muller C. 14
Murphy SB. 10
Murray C. 67
Nakae S. 46
Nakanishi K. 76
Natoli V. 64
Naves A. 87
Nehlsen-Cannare. 58
Neuland CY. 67
Neville ME. 53
Neville ME. 54
Newman RA. 29
Nowinski RC. 35
Noworolska A. 8
Okamoto M. 83
Okumura H. 46
Onoue K. 75
Oscier D. 6
Ozato K. 36
Parish CR. 30
Parker JW. 13
Pavlovsky S. 2
Pawelec G. 14
Pawelec GP. 80
Peller S. 62
Pessano S. 18
Pierres M. 33
Poggio E. 74
Pollastri E. 87
Polliack A. 66
Potomski J. 8
Prendiville MA. 34
Prochazka J. 82
Puig N. 87
Ralph P. 60
Raneletti FO. 64
Raso V. 68
Rehbein A. 80
Rendine S. 74
Revillard JP. 24
Richter R. 8
Rose M. 12
Rosse C. 85
Rossen RD. 72
Rossi GB. 25
Rovera G. 18
Rudolf M. 84
Rumke HC. 6
Sachs DH. 36
Sackmann-Muriel. 2
Salisbury JG. 57
Samarut C. 24
Sandrin MS. 30
Santos I. 5
Santurbano B. 25
Sartoris A. 74
Scavennec J. 4
Scavennec J. 7
Schneider C. 27
Schuch K. 14
Schulte R. 40
Schwemmle K. 86
Sen L. 2
Sen L. 5
Shaked U. 62
Shapiro IM. 19
Sherman LA. 31
Shiho O. 76
Silvian I. 52
Simon MM. 28
Skubitz KM. 47
Sobeslavsky C. 82
Solomon A. 70
Spira G. 52
Spit BJ. 16
Springer TA. 43
Stehlin JS. 72
Stein H. 27
Stockbauer P. 26
Stoliar A. 21
Strong DM. 67
Suemura M. 76
Sugamura K. 79
Sugimura K. 76
Sun D. 44
Sun G. 73
Sutherland DR. 29
Svennevig JL. 81
Tada K. 46
Tam MR. 35
Tanaka Y. 79
Taylor CR. 13
Teillaud JL. 22
Ten Berge RJ. 6
Teranishi T. 75
Terhorst C. 34
Ternynck T. 42
Thien SL. 6
Titeux M. 56
Torres BA. 38
Trotter J. 40
Trowbridge IS. 17
Trowbridge IS. 40
Trowbridge IS. 41
Trucco M. 18
Tsuchiya S. 46
Tsukuda K. 19
Ubels-Postma J. 9
Unanue ER. 20
Unanue ER. 48
Vainchenker W. 56
Van Basten CD. 16
Van Beek AA. 9
Van Der Reijden. 6
Van Heerde P. 9
Verbi W. 27
Volsky DJ. 19
Von Dem Borne A. 6
Von Dem Borne A. 9
Wallen WC. 67
Waters H. 69
Weissgarten J. 62
Wernet P. 14
Wernet P. 80
White JM. 12
Wilkes BM. 88
Wilms K. 14
Wolf A. 71
Xue Z. 73
Yamamoto JK. 38
Yamamura Y. 76
Yamanaka N. 11
Yasmineh WG. 45
Zagury D. 42
Zahn G. 28
Zeijlemaker WP. 9
Zhen YS. 47
Zheng S. 73
Zhou S. 73
Zhu X. 73
Ziegler A. 80
Zittoun R. 65

# VIDEOTAPES

## ON CURRENT TOPICS IN CANCER RESEARCH

A pilot project of the International Cancer Research Data Bank (ICRDB) Program of the National Cancer Institute

*Three series are available . . .*

### THE RELATION OF CARCINOGEN ACTION ON DNA TO CELL TRANSFORMATION

| | | |
|---|---|---|
| PETER MAGEE<br>Fels Research Institute | *Keynote Address* | #VK01<br>28 min. |
| JAMES K. SELKIRK<br>Oak Ridge National Laboratories | *Metabolic Activation and Macromolecular Binding of Chemical Carcinogens* | #VK02<br>51 min. |
| PHILIP C. HANAWALT<br>Stanford University | *Cellular Responses to Damaged DNA* | #VK03<br>54 min. |
| CHARLES HEIDELBERGER<br>University of Southern California | *Mutagenesis and Oncogenic Transformation of Mouse Embryo Cells* | #VK04<br>54 min. |
| FRED RAPP<br>Milton S. Hershey Medical Center | *The Interaction of Herpesviruses and Host Cells Leading to Latency or Transformation* | #VK05<br>52 min. |
| | *Panel Discussion* | #VK06<br>31 min. |

### MECHANISMS OF METASTASIS

| | | |
|---|---|---|
| ISAIAH FIDLER<br>Frederick Cancer Research Center | *The Heterogeneous Nature of Cancer Metastasis and Implications for Therapy* | #VB01<br>47 min. |
| GEORGE POSTE<br>Smith, Kline and French Laboratories | *Phenotypic Analysis of Metastatic Cell Populations* | #VB02<br>42 min. |
| LANCE LIOTTA<br>National Cancer Institute | *Tumor Cell Invasion of Basement Membranes and Extracellular Matrices* | #VB03<br>33 min. |
| EVERETT SUGARBAKER<br>Miami Cancer Institute | *Some Clinical Characteristics of Metastasis in Man* | #VB04<br>41 min. |

### AUTOMATED CYTOLOGY

| | | |
|---|---|---|
| Part One: Principles and Techniques | | #VB05<br>56 min. |
| Part Two: Biological Applications | | #VB06<br>52 min. |

VIDEOTAPES ON CURRENT TOPICS IN CANCER RESEARCH are in the 3/4" U-matic format and can be played on video equipment which accepts the NTSC standard (the standard for videotapes produced in the U.S.). The two Automated Cytology tapes (#VB05 and #VB06) are also available in the PAL format.

The videotapes are available on a loan basis. If you would like to schedule viewing for your group, or for more information, please write to:

Videotape Coordinator
ICRDB Program
Westwood Building, Room 10A18
Bethesda, MD 20205

Please specify three choices for viewing dates, and the tapes desired.

# Keep Up with the Cancer Literature

## Each Month
## You Can Receive Abstracts
## Covering Your Specialty Area

- This convenient service — called Auto SDI* — is as near as your nearest biomedical library. Discuss your research interests with the librarian who will design an appropriate search strategy.
- Abstracts of the latest published literature are searched automatically each month and those related to your interests are delivered to you on a regular basis.
- The abstracts you receive are selected from more than 4,000 monthly entries made into CANCERLIT — the extensive cancer literature data base of the National Cancer Institute.

## Talk With Your Librarian
## About the Auto SDI Service TODAY.

*Auto SDI stands for Automatic Selective Dissemination of Information. It is a service provided to you, at minimal cost, by the International Cancer Research Data Bank (ICRDB) — a part of the National Cancer Institute.

**U.S. DEPARTMENT OF COMMERCE**
**National Technical Information Service**
5285 Port Royal Road
Springfield, Va. 22161

OFFICIAL BUSINESS

Penalty for Private Use, $300

**PRINTED MATTER**

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF COMMERCE
COM-211

THIRD CLASS
BULK RATE

U.S.MAIL

CB-17

**CANCERGRAMS are distributed for the International Cancer Research Data Bank (ICRDB) by the National Technical Information Service (NTIS). CANCERGRAMS are available from NTIS on a standing order basis at $2 each for North American Continent addresses and $3 each for other addresses. An NTIS deposit account is required. For a list of subject categories or other information, please write to:**

**Subscription Section**
**National Technical Information Service**
**5285 Port Royal Road**
**Springfield, VA 22161**

**NOTICE OF MAILING CHANGE**

☐ Check here if you wish to discontinue receiving this publication.

☐ Check here if your address has changed and you wish to continue receiving this publication. (Be sure to furnish your complete address including zip code.)

Tear off cover with address label still affixed and send to:

Computer Support Center
ICRDB Program
IIT Research Institute
10 West 35th Street
Chicago IL. 60616

CB 17/82/09

NCI/ICRDB/CB17 82/09

PB82-931809

# ICRDB CANCERGRAM

# IMMUNOBIOLOGY AND CANCER

## Identification and Characterization of Immune Cells

SERIES CB17 No. 82/09

SEPTEMBER, 1982

This Cancergram is a service of the INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM of the U.S. National Cancer Institute. Every few weeks, an updated Cancergram containing abstracts of selected cancer-related articles recently published in more than 3000 journals, and dealing with the topic indicated by the above title, is sent to researchers working in this area. These researchers are identified on the basis of the description of their current research project that has been submitted to the ICRDB Program, directly or via granting agencies.

This Cancergram is prepared by the Cancer Information Dissemination and Analysis Center (CIDAC) for Virology, Immunology, and Biology. ***If this Cancergram is useful and valuable, please send your comments to the CIDAC address below, since future editions depend on user satisfaction and user needs:***

CIDAC FOR VIROLOGY, IMMUNOLOGY, AND BIOLOGY
SCIENCE INFORMATION SERVICES
FRANKLIN INSTITUTE RESEARCH LABORATORIES
20TH AND RACE STREETS
PHILADELPHIA, PA 19103

NEWARK PUBLIC LIBRARY

OCT 1 4 19..

U. S. GOVT. PUBS.
DEPOSITORY 376

PDQ (PROTOCOL DATA QUERY) - A NEW ONLINE CANCER DATABASE WILL BE AVAILABLE THIS FALL! PDQ LISTS THERAPY PROTOCOLS PLUS ADDRESSES AND PHONE NUMBERS OF CLINICAL INVESTIGATORS. CONTACT ICRDB FOR DETAILS.

*In this issue:*


- CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS..... 1-11
- DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS..... 12-23
- LYMPHOCYTE AND DIFFERENTIATION ANTIGENS..... 24-32
- CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION..... 33-43
- EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS..... 44-46
- OTHER RELATED STUDIES..... 47-58


U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service • National Institutes of Health • National Cancer Institute

HE 20.3173/2:

## CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS

### 1. 'TARGET' CELLS, CELLULAR PHENOTYPES, AND LINEAGE FIDELITY IN HUMAN LEUKAEMIA.

Greaves MF
Membrane Immunology Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England
J Cell Physiol; Suppl1:113-125 1982

Features of leukemic phenotypes in relation to normal hemopoietic differentiation were investigated in a study developed as a part of a routine immunodiagnostic service for leukemia in the United Kingdom (UK). Leukemic samples (heparinized blood, lymph node biopsies, cerebrospinal fluid, and peritoneal aspirates) were obtained from referring hospitals throughout the UK. A presumptive normal sequence of antigen (and other marker) expression in T cell differentiation is presented. The scheme is based upon reported antigenic heterogeneity of cortical and medullary thymocytes and subsets of blood T cells. The corresponding maturation 'positions' of 95 leukemic T cell phenotypes analyzed are presented. T-acute lymphoblastic leukemia (T-ALL), and T-non-Hodgkin's lymphoma in childhood 'correspond' to early or late thymocyte populations while T cell leukemias or lymphomas of older (greater than 35 yr) patients diagnosed as cutaneous lymphoma or leukemia, chronic lymphocytic leukemia, prolymphoblastic leukemia, or lymphoblastic lymphoma, all had 'mature' T phenotypes. The phenotypes that were documented in non-T-ALL are summarized. The majority of complementary ALL that do not synthesize detectable mu chain nevertheless have rearranged mu chain genes as revealed by molecular hybridization studies. Alterations in phenotype during leukemia progression or relapse may provide some evidence for distortion of 'normal' genetic programs as well as revealing the lineage affiliations of various clonogenic populations. Alterations in the latter population may indirectly indicate the possible target cell population involved. (89 Refs)

### 2. ACUTE LYMPHOCYTIC LEUKEMIA: BIOLOGICAL MARKERS OF CLINICAL RESPONSE.

Mauer AM, Bowman WP, Dow LW, Look AT, Williams D
St. Jude Children's Res. Hosp., Memphis, TN, 38101
J Cell Physiol; Suppl1:127-132 1982

New biological observations that have clinical importance in the treatment of acute lymphoblastic leukemia (ALL) are presented, and current therapeutic problems are described. One hundred and thirty-five patients were entered into the treatment program for standard-risk patients; 101 had WBC counts less than 25,000/cubic mm (mm3) and none of those patients have relapsed. Nine of 34 patients with counts greater than 25,000/mm3 have already relapsed. Proliferative activity was assessed by determining the tritiated thymidine labeling index of blood and bone marrow leukemic blast cells. A significant difference in treatment outcome was found when the group of patients was divided into two parts based on higher or lower level of proliferative activity in the blood and bone marrow blast cells. Bone marrow treatment failed in 42% of patients with labeling index (LI) less than 6%, and in 74% of patients with LI greater than 6%. Initial blast cell karyotypes of 135 patients with ALL were analyzed. The patients with greater than 50 chromosomes have had only two treatment failures. Only 70% of 28 patients with pseudodiploid karyotypes achieved initial remission and 19 have experienced treatment failure. Leukemic blast cell DNA content was analyzed by flow microfluorometry and the data was correlated with the results of the cell surface marker studies. Cells having hyperdiploid DNA content were more likely to have an expression of surface common ALL antigen. However, those cells having T-lymphocyte markers rarely have abnormal DNA content detectable by flow cytometry. These observations suggest the existence of an interrelationship among studied biological features associated with treatment response. (12 Refs)

### 3. ACUTE LEUKEMIA WITH BURKITT'S LYMPHOMA CELLS IN TWO JAPANESE CHILDREN: CLINICAL MANIFESTATIONS AND CELL SURFACE MARKERS.

Kusakari A, Nakazawa S, Takane K, Yamada K
Dept. Pediatrics, Tokyo Metropolitan Children's Hosp., 1-3-1 Umezono, Kiyose City, Tokyo, Japan
Rinsho Ketsueki; 22(12):1962-1970 1981

Two cases of B-cell acute lymphoblastic leukemia (B-cell ALL) that showed cytological characteristics of Burkitt's lymphoma cells are reported. A 3 yr 5 mo old boy complained of vomiting, abdominal pain, fever, and had hyperuricemia. An extensive infiltration of peroxidase negative lymphoblastic cells was noted and the patient was diagnosed for ALL. Blast cells showed basophilic staining with several vacuoles on Wright-Giemsa staining. Surface immunoglobulin of IgM was detected in 84% of blast cells. Positive reactions against anti-B antigen (Ia-like antigen) serum (100%) and anti-common ALL antigen serum (38%) were noted, and the disease was determined to be B-cell ALL. Treatment with prednisolone and vincristine was initiated. Despite a transient cardiac arrest due to hyperkalemia, a complete remission was seen. Four wk later, however, the patient developed meningeal and testicular leukemia and refractory hematological relapse. The patient did not respond to further treatment and expired in 5.5 mo. A 3 yr 3 mo old boy complained of headache, abdominal pain, and pain in the right thigh. A massive infiltration of bone marrow by blast cells with morphological features similar to those in the first patient was observed. Cell surface analysis led to diagnosis of B-cell ALL. IgM was detected in 100% of blast cells, and positive reaction against the same antigens as in the first patient were observed. Meningeal leukemia also occurred. Prednisolone and vincristine treatment was discontinued due to ileoileal intussusception followed by diffuse peritonitis on day 1 of therapy. In 3 wk, a complete remission was seen. In 5 wk, however, refractory hematological relapse developed and the patient died of pneumonia after 3.5 mo. Both patients showed a high rate of surface Ig appearance, negative RBC antibody complement rosette, positive B-antigen (Ia-like), and weakly positive common ALL antigen. These observations suggest that B-cell ALL may have a pathogenesis similar to Burkitt's lymphoma. (31 Refs) (In JPN)

### 4. ACUTE MONOCYTIC LEUKEMIA: A SURFACE MARKER STUDY.

Mirchandani I, Tabaczka P, Palutke M
Dept. Pathology, Wayne State Univ. Sch. Medicine, 540 E. Canfield Ave., Detroit, MI, 48201
Am J Hematol; 12(2):139-147 1982

Thirteen cases of acute monocytic leukemia (AMoL) were studied morphologically, cytochemically, and immunologically in an attempt to determine similarities and/or differences between acute monocytic and lymphocytic leukemias. Single class surface immunoglobulins (IgG kappa) were seen in six cases. These markers are thought to represent serum immunog-

lobulins attached to the leukemic monocytes via the receptors for the Fc portion of immunoglobulin and are not synthesized by the cells as is the case with B lymphocytes. Receptors for complement were also noted. It appears that surface immunoglobulins and receptors for the Fc portion of the immunoglobulin and complement, which are found on several classes of normal lymphocytes and monocytes, may also be found on leukemic monocytes. Antisera to B lymphocytes, detecting HLA-DRw antigens, also reacted with some of the leukemic monocytes. (Author abstract) (34 Refs)

## 5. T-CELL CHRONIC LYMPHOCYTIC LEUKEMIA: REPORT OF A CASE STUDIED WITH MONOCLONAL ANTIBODY.

**Aisenberg AC, Wilkes BM, Harris NL, Koh HK**
**Massachusetts General Hosp., Boston, MA, 02114**
**Am J Med; 72(4):695-699 1982**

A previously healthy 74-yr-old woman presented with T-cell chronic lymphocytic leukemia, lymphadenopathy, hepatosplenomegaly and a mediastinal mass. The circulating lymphocytes were small to medium in size (some with convoluted nuclei) and E rosette-positive; they could be assigned to the inducer-helper subset of T cells with the aid of monoclonal antisera. These cells reacted with OKT3, which detects peripheral T cells; OKT4, which detects the inducer-helper subset of T cells; and OKT11, which detects the sheep cell receptor. It is noteworthy that they were also positive for the Ia-like antigen found on T cells only after activation. Microscopic examination of a lymph node biopsy specimen revealed a diffuse pattern of pleomorphic large cells characteristic of the T-cell lymphomas and lymphocytic leukemias reported from Japan. However, the lymph node cells lacked the T-cell differentiation antigens present on the circulating lymphocytes. The findings of this case provide insight into the pathogenesis of this unusual disorder and are relevant to our understanding of the spectrum of surface antigens in the more common malignant lymphomas. (Author abstract) (34 Refs)

## 6. DIFFERENTIAL LOSS OF T LYMPHOCYTE MARKERS IN ADVANCED CUTANEOUS T CELL LYMPHOMA.

**Holden CA, Staughton RC, Campbell MA, MacDonald DM**
**(c/o MacDonald) Dept. Dermatology, Guy's Hosp., St. Thomas' St., London SE1 9RT, England**
**J Am Acad Dermatol; 6(4,part1):507-513 1982**

Tumor biopsies from a 71-yr-old man with disseminated cutaneous T-cell lymphoma (CTCL) was assayed for T-cell markers. The patients showed multiple cutaneous tumors, hepatomegaly, lymphadenopathy, and early bone marrow involvement. The CTCL cells contained antigens reacting with antisera to human T-lymphocyte antigen and a monoclonal antiserum (OKT3), but has lost their RBC rosetting capacities and acid alpha-naphthyl acetate esterase (ANAE) activity. The CTCL cells did not express antigens associated with helper or suppressor T-cells (identified using OKT4 and OKT8 antisera, respectively). The use of monoclonal antisera against T-cell surface antigens may eventually provide antigenic profiles of the malignant cells present in CTCL of differing degrees of aggressiveness, leading to more accurate prognoses and earlier recognition and treatment. (19 Refs)

## 7. IMMUNOLOGIC CHARACTERIZATION OF A HELPER T-CELL LYMPHOMA.

**Gramatzki M, Dolan MF, Fauci AS, Maples JA, Bonnard GD, Strong DM**
**(c/o Strong) Tissue Bank, Naval Medical Res. Inst., Bethesda, MD, 20814**
**Blood; 59(4):702-708 1982**

The lymphocytes of a patient with a T-cell non-Hodgkin's lymphoma with peripheral blood involvement and polyclonal hypergammaglobulinemia were characterized in terms of surface markers and immunologic functions. Using the fluorescence-activated cell sorter and employing various monoclonal antibodies against T-cell surface antigens, it was shown that almost all of the patient's peripheral blood lymphocytes were positive for OKT4 and 9.3, antibodies that recognize helper T-cell subset. The circulating lymphoma cells had typical characteristics for T cells; they formed spontaneous rosettes with sheep erythrocytes and stained with the pan T-cell antibodies 9.6 and 10.2, but did not react with other anti-T-cell monoclonal reagents such as OKT3, UCHT-1, and 3A1. The cells appeared to be mature by the fact that they did not stain with OKT6, and terminal deoxynucleotidyl transferase was undetectable. Functionally, they were able to provide 'help' for antibody production, and they could be stimulated to produce moderate amounts of interleukin-2, while unable to proliferate in response to mitogens. Morphologically, some of the lymphocytes showed a deeply cleaved nucleus. (Author abstract) (53 Refs)

## 8. NON-HODGKIN LYMPHOMA OF THE SO-CALLED PRIMARY NEURAXIS TYPE. IMMUNOLOGICAL STUDY OF 4 CASES.

**Chazot G, Pialat J, Touraine F, Trillet M, Schott B**
**Service de Neurologie, Hopital Neurologique, 59, boul. Pinel, F 69003 Lyon, France**
**Rev Neurol (Paris); 137(4):291-295 1981**

Blood cells from four patients (38-62-yr-old) with cerebral neuraxis type lymphomas were studied immunologically. The three frontal lymphomas consisted of large centrofollicular cells while a paraventricular tumor was a type B immunoblastosarcoma. In 3/4 cases, T-cell deficiency was observed despite absence of recent radiotherapy, chemotherapy, or corticotherapy. Electrophoresis and immunoelectrophoresis showed no immunoglobulin anomalies. Cellular immunity of tumor cells was examined in 3/4 cases. In all three cases, surface characteristics of tumor cells corresponded with a predominant B-cell population. The observed T-cell deficiency was comparable to that found in patients with cerebral lymphomas developing during the course of immunosuppression following organ transplants. It was suggested that deficient T-cell immunity allowed the proliferation of the B-lymphocyte clone. Hypotheses are presented which may in part explain the development of the cerebral lymphomas. (12 Refs) (In FRE)

## 9. A HUMAN PLASMA CELL LINE: INDUCTION AND CHARACTERIZATION.

**Miller CH, Carbonell A, Peng R, Paglieroni T, MacKenzie MR**
**Dept. Pathology, Sch. Medicine, Univ. California, MS-1, Room 3453, Davis, CA, 95616**
**Cancer; 49(10):2091-2096 1982**

A stable line of IgG K producing human plasma cells was established from a myelomatous human bone marrow using conditioned media from a rapidly metabolizing lymphoblast line, RPMI 4098. Growth in RPMI 1640 (15% fetal calf

serum) at 6% CO2 promoted a 62-hr doubling time with a preferred cell concentration of 1 x 10(6)/mL. Surface marker studies showed: no receptors for sheep erythrocytes, no surface immunoglobulins, variable number of cells bearing complement receptors and 83% bearing Fc receptors. Although transmission electron micrographs demonstrated a poorly developed endoplasmic reticulum, radioimmunoassay showed 23 ng IgG and 28.7 ng Kappa were produced by 1 x 10(6) cells in 72 hr. Further, the cells are lipase, esterase and Epstein-Barr nuclear antigen negative. ASG banding showed a total chromosome number that varied from 46-49. Since the number of human plasma cell lines is limited, it is felt that this line will augment the immunobiological study of human myeloma. (Author abstract) (16 Refs)

### 10. ANALYSIS OF CARBOHYDRATE DETERMINANTS ON MEMBRANES OF LEUKEMIC LEUKOCYTES USING NATURALLY OCCURRING MONOCLONAL HUMAN ANTIBODIES (COLD AGGLUTININS).

**Dorken B, Roelcke D, Bohn B, Hunstein W**
**Medizinische Universitats-Poliklinik, 69 Heidelberg, W. Germany**
**Protides Biol Fluid Proc Colloq; 29:623-626 1982**

The reaction of monoclonal anti-I, -i, -Pr1, -Pr2, -Gd and the monoclonal cold agglutinin (CA) Sa with cells from patients with acute leukemia was examined. The RBC-autoantigens I, i, Pr1, Pr2, GD and SA were found on blasts of 25 adult patients with acute leukemia [10 myelocytic (AML), 2 promyelocytic, 4 myelomonocytic (AMML), and 9 lymphoblastic (ALL)]. Expression of three antigens was associated with the cell type of leukemia: I, i, and Pr1 were not detectable or only weakly expressed on AML cells, whereas on ALL cells the antigens occurred to a greater extent. There was, however, considerable heterogeneity in the ALL group. The proportion of stained cells was often less than 30%. The difference in the anti-i reaction between AML and ALL was less striking after neuraminidase treatment, indicating that more antigenic determinants became available by enzymatic removal of N-acetyl-neuraminic acid. In contrast to AML cells, there was a very strong reactivity of anti-I, anti-i, and anti-Pr1 with AMML cells. Since it is often difficult to distinguish AMML and AML morphologically, the CA may be useful. No correlation with cell type was found in the case of Pr2, Gd, and Sa. Study of cultured PHA-stimulated T lymphocytes revealed that the antigen expression varied concomitantly with the culture periods. The results suggested that i, Gd, and Sa, in contrast to Pr1, are preferentially expressed on proliferating cells. (8 Refs)

### 11. THE HANDBOOK OF CANCER IMMUNOLOGY. VOLUME 6: LYMPHOID CELL SUBPOPULATIONS: STRUCTURE, FUNCTION, AND INTERACTIONS.

**Waters H**
**NIH, Bethesda, MD**
**The Handbook of Cancer Immunology. Volume 6: Lymphoid Cell Subpopulations: Structure, Function, and Interactions. New York, Garland STPM Press, 314 pp., 1981.**

Lymphoid cell subpopulations are discussed in relation to cellular interactions in metastasis, role of immunosuppressants in lymphocyte function, human T cell subclasses with IgG and complement receptors, age-related changes in marrow stem cells, functions of atypical lymphocytes, biology of marrow-dependent cells in mice, pathogenesis of plasma cell tumors, functional stimulation of T cells with protein antigens, effects of lymphokines on tumor cells, and perspectives of lymphocyte production and cellular traffic in the bone marrow. (1334 Refs)

## DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS

### 12. EXPRESSION AND DYNAMICS OF MEMBRANE IMMUNOGLOBULINS.

**Pernis B, Roth P**
**Dept. Microbiology, Coll. Physicians and Surgeons, Columbia Univ., New York, NY**
**Pharmacol Rev; 34(1):65-72 1982**

Membrane immunoglobulins on B lymphocytes, membrane IgD, simultaneous expression of messenger IgM and IgD, and internalization or shedding of cross-linked membrane IgM and IgD in human B lymphoid cells are discussed. Important information on the effects of interactions with messenger Ig on B cell differentiation has been derived from experiments in which anti-immunoglobulin antibodies could block specific antibody production in an in vitro immune response as well as differentiation to immunoglobulin-secreting cells in mitogen-activated lymphocyte cultures. (162 Refs)

### 13. THE INFLUENCE OF ANTIGEN DENSITY AND A COMPARISON OF IGG AND IGM ANTIBODIES IN THE ANTI-COMPLEMENTARY MODULATION OF LYMPHOCYTIC SURFACE IMMUNOGLOBULIN.

**Gordon J, Anderson VA, Robinson DS, Stevenson GT**
**Lymphoma Res. Unit, Tenovus Res. Lab., Southampton General Hosp., Tremona Road, Southampton SO9 4XY, England**
**Scand J Immunol; 15(2):169-177 1982**

Experiments were carried out to determine the influence of antigen density on anti-complementary modulation, defined here as the conferring by anti-immunoglobulin (Ig) of resistance to lysis of guinea pig L2C leukemic lymphocytes through anti-Ig plus syngeneic complement (C). Populations of leukemic cells varied widely in their quantitative expression of surface membrane Ig as judged by the binding to cells of 125I-labeled Fab' fragments from anti-Ig, and a good correlation between the bulk antigen density and the percentage of cells lysed by anti-Ig plus C was obtained ($p = 0.02$). In the presence of 10 mM sodium azide, which has been shown to diminish the modulation occuring during simultaneous incubations with anti-Ig and C, this correlation was even stronger (p less than 0.001). No zone could be defined in which the level of surface Ig expression was sufficient to serve complement lysis but too low for modulation. Furthermore, both the degrees and rates of modulation occurring on incubation with antibody at 37 C, either before C addition or in the presence of lytic C, were similar for populations of high, low, or intermediate antigen density. Separation of cells by their size or density failed to yield populations differing in either their susceptibility to humoral killing through anti-Ig or their modulating capacity. IgG and IgM antibodies to the L2C cell surface Ig evoked similar levels of killing with syngeneic C, and when compared for their ability to promote anti-complementary modulation, no difference was revealed in either the rate or degree of modulation occurring during incubations at 37 C with the two isotypes. The findings are discussed with particular reference to observations on the modulation of mouse thymus leukemia (TL) antigens. (Author abstract) (38 Refs)

## 14. DETECTION OF SURFACE IMMUNOGLOBULINS OF HUMAN LYMPHOID CELLS: A COMPARATIVE STUDY OF LIVE AND FIXED CELLS USING A DIRECT IMMUNOPEROXIDASE PROCEDURE.

Laurent G, Gourdin MF, Reyes F
(c/o Reyes) Inserm U.91, Hopital Henri Mondor, 94010 Creteil, France
J Clin Pathol; 35(2):139-143 1982

Surface immunoglobulins (Ig) of normal and malignant lymphoid cells were detected on prefixed, smeared (Method A) and live (Method B) cell suspensions; the results were compared with regard to staining patterns, specificity and sensitivity. In both methods surface Ig were detected by a direct immunoperoxidase procedure using conjugated purified antibody. Although Method A has practical advantages, Method B is more sensitive. The reasons for this discrepancy are discussed in relation to surface Ig denaturation and redistribution. (Author abstract) (21 Refs)

## 15. FC RECEPTORS FOR IGE ON MOUSE MACROPHAGES AND MACROPHAGE-LIKE CELL LINES.

Boltz-Nitulescu G, Plummer JM, Spiegelberg HL
Inst. General Experimental Pathology, Univ. Vienna, Wahringerstrasse 13, A 1090 Vienna, Austria
J Immunol; 128(5):2265-2268 1982

Murine alveolar and peritoneal macrophages (AMphi, PMphi) and Mphi-like cultured cell lines were analyzed for IgE Fc receptors by rosette formation with mouse IgE-sensitized red cells and by binding of radiolabeled mouse IgE. A mean of 90.4% AMphi, 56.9% PMphi, 93.4% P388D1, 81.2% J744.1, 15.6% WEH13, 54.7% WR19M.1, 52.3% RAW264.7, and 19.5% RAW309Cr.1 Mphi-like cells formed IgE rosettes. The rosettes were specific for native mouse IgE and were inhibited by mouse IgE but not mouse IgG, IgA, IgM, or heat-denatured mouse IgE. Rat IgE, but not human IgE, induced rosettes and inhibited mouse IgE rosettes. Trypsin treatment of the Mphi abolished IgE rosette formation. Mouse IgE bound to P388D1 Mphi-like cells with a KA of 7.6 +-0.2 x 10(6) M-1 to 3.3 +-0.9 x 10(5) binding sites. After 30 min of incubation at 37 C, 30 to 45% of AMphi, P388D1, and J774.1 Mphi-like cells ingested erythrocytes sensitized with IgE but not unsensitized erythrocytes. The data indicate that mouse Mphi bear Fc receptors specific for IgE that mediate phagocytosis of IgE-sensitized erythrocytes. (Author abstract) (29 Refs)

## 16. CHARACTERIZATION OF TWO SUBSETS OF HUMAN TGAMMA CELLS.

van de Griend RJ, Ten Berge I, Tanke HJ, Roos D, Schellekens PT, Melief CJ, Jeljemaker WP, Astaldi A
(c/o Roos) Central Lab., The Netherlands Red Cross Blood Transfusion Service, P.O. Box 9190, 1006 AD Amsterdam, The Netherlands
J Immunol; 128(5):1979-1985 1982

Normal human E rosette-forming, Fc-IgG receptor-bearing cells (so-called Tgamma cells) were separated into two functionally different subpopulations. Both subpopulations bind the monoclonal antibody OKM1 (directed against an antigen present also on monocytes and granulocytes). The first subpopulation accounts for about 70% of the total Tgamma cell population, does not bind OKT3 (a monoclonal antibody directed against an antigen present on most T lymphocytes), and displays strong killer (K) cell and natural killer (NK) cell activity. The second subpopulation accounts for about 30% of the total Tgamma population, binds both OKT3 and OKM1 (confirmed with a double-labeling assay), and displays low K and NK cell activity. Each subset contained less than 10% null cells. Comparison of Tgamma cell populations obtained by adherence to a monolayer of IgG-coated human erythrocytes or by rosette formation with these cells revealed that pure Tgamma cells with normal killer cell and natural killer cell activity were best obtained with the monolayer technique. Comparison of the enzymic and functional profile of Tgamma cells, monocytes and granulocytes, as well as changes during culture of these cells in vitro, failed to indicate a relationship between Tgamma cells and cells of the myelomonocytic lineage. (Author abstract) (41 Refs)

## 17. RECEPTORS FOR IGA ON RABBIT LYMPHOCYTES. II. CHARACTERIZATION OF THEIR BINDING PARAMETERS FOR IGA.

Stafford HA, Knight KL, Fanger MW
Dept. Microbiology and Medicine, Dartmouth Medical Sch., Hanover, NH, 03755
J Immunol; 128(5):2201-2205 1982

The specificity of rabbit receptors for IgA (RFcalpha) was investigated on lymphocytes isolated from the Peyer's patches and spleen. Specificity was determined by the inhibition of IgA rosette formation with intact and proteolytic fragments of rabbit and human secretory IgA (SIgA), human myeloma proteins, and secretory component. RFcalpha bound human SIgA as efficiently as rabbit SIgA. Of the human IgA tested, RFcalpha preferentially bound to the IgA2 subclass and mostly avidly to a multimeric IgA molecule. In addition, the site of RFcalpha-IgA interaction was localized to the Calpha2 domain in the Fc portion of IgA. RFcalpha on spleen lymphocytes showed the same pattern of binding specificity toward the human IgA subclasses as the RFcalpha on lymphocytes from Peyer's patches. However, differences between the spleen and Peyer's patches were observed in the interaction of RFcalpha and the rabbit IgA subclasses. RFcalpha on lymphocytes from the Peyer's patches bound the rabbit IgA-g subclass more efficiently than the rabbit IgA-f subclass, whereas the converse was true for the spleen RFcalpha. Human secretory component inhibited IgA but not IgG or IgM rosette formation as a result of its interaction with lymphocytes. These studies suggest: (1) that there may be two types of RFcalpha expressed by lymphocytes in certain tissues, and (2) that there are two closely associated receptors on the lymphocyte - one specific for secretory component and the other for structures within the Calpha2 domain of IgA. (Author abstract) (20 Refs)

## 18. HUMAN T CELL SUBCLASSES WITH IGG AND COMPLEMENT RECEPTORS.

Chiao JW
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
The Handbook of Cancer Immunology Volume 6: Lymphoid Cell Subpopulations-Structure, Function, and Interactions. Waters H, ed. New York, Garland STPM Press, 314 pp., 1981.

Studies on the nature of T lymphocytes possessing both commonly used markers (IgG or complement) and once referred to as cells having both B and T markers, now considered T-lymphocyte subclasses, are presented. Topics include tissue distribution and presence in lymphoid neoplasms, functional properties (antibody dependent cellular-cytotoxicity), suppressor and helper cell functions, activated T cells, and mitogenic responses and other functions. Cell morphology and the development of T cell subclasses are discussed. (160 Refs)

## 19. INTERACTION OF PARTICLE-BOUND [125I]C3B, THE THIRD COMPONENT OF COMPLEMENT, WITH SPECIFIC RECEPTORS ON HUMAN B-LYMPHOBLASTOID CELLS (RAJI).

Frade R, Strominger J

Institut de Cancerologie et d'Immogenetique, 16 avenue Paul-Vaillant Couturier, 94800 Villejuif, France

Immunol Lett; 3(3):173-178 1981

The interaction between particle-bound C3b and specific C3b receptors present on human B-lymphoblastoid cells was studied, taking advantage of the high density of the complex formed between C3b receptors on B-lymphoblastoid cells and C3b coated to zymosan particles. The process had an apparent dissociation constant equal to 10(-7) M. Results indicate that C3b associated to particles has a higher affinity for specific C3b receptors than soluble C3b. Analysis of of the dissociation rate of particle-bound C3b-C3b receptor complexes suggested that a cooperative effect was induced at the cell surface by particle-bound C3b but not by soluble C3b. Possible explanations of these results are discussed. (25 Refs)

## 20. RECEPTORS FOR T-CELL GROWTH.

Kipp DE, Askonas BA

Immunology Div., MRC Natl. Inst. Medical Res., Mill Hill, London NW7 1AA, England

Nature; 296(5859):707 1982

T-cell growth factors (TCGF) and their biological significance are discussed. While the resting T-cell is unresponsive to TCGF, mitogen- or antigen-activated T-cells do respond. All of the non-T-cell human neoplastic cell lines and 90% of human T-cell human neoplastic cell lines studied have failed to bind TCGF in vitro. Transformed cell lines may have lost expression of TCGF receptors or may have been derived from early T-cells that had not yet expressed receptor activity. (10 Refs)

## 21. STUDIES ON ANTIGENS OF A LEUKEMIC NULL-CELL LINE (NALL-1). I. STIMULATORY CAPACITY IN MIXED LYMPHOCYTE CULTURE.

Uno J

Second Dept. Internal Medicine, Okayama Univ. Medical Sch., Okayama, Japan

Okayama Igakkai Zasshi; 93(5/6):481-487 1981

A one-way mixed lymphocyte reaction between lymphocytes from normal human donors and mitomycin C-treated cells from a human leukemic null-cell line (NALL-1) was investigated. Human leukemic T-cell and B-cell lines, an Epstein-Barr virus (EBV)-negative Japanese Burkitt's lymphoma line, and two EBV-positive normal B-cell lines were studied in parallel. Normal lymphocytes were stimulated significantly by the cultured null- and B-cells but not by the cultured T-cells. The stimulatory capacity of this null-cell line was approx equal to that of the leukemic, lymphoma, and normal B-cell lines, and was unrelated to the presence of complement receptor, surface immunoglobulin, EBV-associated nuclear antigen, terminal deoxynucleotidyl transferase or the origin of the cell lines. These results suggest that not only leukemic B-cells but also leukemic null-cells have stimulatory determinants in mixed lymphocyte culture. (Author abstract) (21 Refs) (In JPN)

## 22. ABNORMAL MIGRATION OF T LYMPHOCYTE CLONES.

Dailey MO, Fathman CG, Butcher EC, Pillemer E, Weissman I

Dept. Pathology, Stanford Univ. Medical Center, Stanford, CA, 94305

J Immunol; 128(5):2134-2136 1982

Several in vitro T cell clones were markedly deficient in their ability to home to peripheral lymphoid tissue. This was found for an alloreactive noncytolytic clone, a soluble antigen-(KLH)specific line, and cytotoxic clones specific for allogeneic cells and for Abelson virus-induced lymphoma cells. This abnormal circulation pattern was probably caused by the lack of the receptors of the lymphocytes for high endothelial venules (HEV), as implied by the lack of binding of these T cells to HEV in frozen sections of mouse lymph node and Peyer's patches. The loss of surface receptors that are necessary for normal lymphocyte migration may thereby alter the in vivo function of adoptively transferred T cells. (Author abstract) (18 Refs)

## 23. INHIBITION OF HUMAN LECTIN-DEPENDENT CELL-MEDIATED CYTOTOXICITY, NATURAL KILLER-LIKE CYTOTOXICITY, AND CYTOTOXIC T-LYMPHOCYTE-MEDIATED CYTOLYSIS BY XENOANTISERA RAISED AGAINST CONCANAVALIN A-STIMULATED HUMAN LYMPHOCYTES.

Devlin JJ, Phaneuf JD, Granger GA

Dept. Molecular Biology and Biochemistry, Univ. California, Irvine, CA, 92717

Cell Immunol; 68(1):64-74 1982

This report describes the in vitro inhibition of several classes of human lymphocyte-mediated lysis by antisera from mice and rats immunized with concanavalin A-stimulated human T-enriched lymphocytes. The inhibitory antibodies in these antisera recognized molecules on the surface of cytotoxic lymphocytes, and did not bind to B-cell lines. Experiments were performed to demonstrate that these antisera were not inhibiting cytolysis by trivial mechanisms such as (i) masking of target cell antigens by anti-target cell antibodies, (ii) agglutinating effector cells, thereby preventing effector-target cell contact, or (iii) toxicity to the effector cells. Dextran dispersion experiments revealed that these antisera inhibit the post-conjugate formation phase of cytolysis mediated by cytotoxic T lymphocytes. These antisera inhibited natural killer-like cytotoxicity and lectin-dependent cell-mediated cytotoxicity as well as lysis mediated by both mixed cell culture-generated cytotoxic T lymphocytes and cytotoxic T-lymphocyte cell lines. These findings suggest that these in vitro systems of cell-mediated lysis may share a common step; however, the different classes of cytolysis may have been inhibited by separate antibodies in the antisera. This rapid reproducible method of generating inhibitory antisera will facilitate the study of the molecules involved in the post-conjugate formation phase of human cytotoxic T-lymphocyte-mediated lysis. (Author abstract) (27 Refs)

## LYMPHOCYTE AND DIFFERENTIATION ANTIGENS

### 24. ENRICHMENT OF HUMAN MARROW LYMPHOCYTES WITH MONOCLONAL ANTIBODIES TO MURINE ANTIGENS.

Landreth KS, Kincade PW, Lee G, Gathings WE, Fu SM
Sloan-Kettering Inst. Cancer Res., 145 Boston Post Road, Rye, NY, 10580
Proc Natl Acad Sci USA; 79(7):2370-2374 1982

Two monoclonal antibodies, prepared against a murine B lymphoma and characterized as binding to a cell surface antigen represented primarily on cells of the B lineage, were found to bind to human hemopoietic cells. These antibodies recognize similar populations of cells in mice and humans. Antibodies from clones 177.17 and 83.4 bound to 6% of human bone marrow nucleated cells. This included all cells with detectable cell surface Ig (sIg+) and those that lack sIg but have detectable cytoplasmic mu (sIg-, cmu+), considered to be the immediate precursors of B lymphocytes (pre-B cells). In addition, these antibodies bound to a subpopulation of T cells and a proportion of null lymphocytes in marrow, spleen, and peripheral blood. An unexpected finding was that established pre-B cell lines were not recognized by these antibodies and possible reasons for this are considered. By using antibody-coated polystyrene plates for cell depletion and recovery, highly enriched preparations of cmu+, sIg- cells have been obtained. These antibodies and enrichment procedures should prove valuable in establishing the minimal requirements for maturation of these putative precursors in vitro, for comparative studies of immunodeficiency/autoimmune diseases in man and experimental animal models, and for monitoring the outcome of therapeutic marrow transplantation. (Author abstract) (24 Refs)

### 25. MONOCLONAL ANTIBODIES AGAINST HUMAN THYMOCYTES AND T LYMPHOCYTES.

Tax WJ, Willems HW, Kibbelaar MD, De Groot J, Capel PJ, De Waal RM, Reekers P, Koene RA
Dept. Nephrology, St. Radboudziekenhuis, Nijmegen, The Netherlands
Protides Biol Fluid Proc Colloq; 29:701-704 1982

The specificity of two cytotoxic monoclonal antibodies (WT 1 and WT 2) produced by the hybridoma technique was analyzed by cytotoxicity, indirect immunofluorescence, and the enzyme-linked immunosorbent assay. WT 1 was reactive with all human thymocytes and all peripheral T lymphocytes, but did not react with any other cell type from peripheral blood. WT 1 also bound to phytohemagglutinin (PHA)-stimulated T cells and to cytotoxic T lymphocytes induced by mixed lymphocyte culture. Monkey lymphocytes also reacted with WT 1 and therefore functional aspects of this antibody, such as immunosuppressive activity, can be studied in the monkey. WT 1 was not mitogenic and did not interfere with PHA stimulation. WT 1 did not block formation of erythrocyte-rosettes and appeared to be unreactive with myeloid progenitor cells. On the other hand, the growth of myeloid colonies was inhibited by prior incubation of bone marrow cells with rabbit complement and monoclonal antibody WT 2. WT 2 was not reactive with peripheral granulocytes or monocytes, and bound to all thymocytes and a small percentage of peripheral lymphocytes. (10 Refs)

### 26. RAT ANTISERA DIRECTED AGAINST ALLOIMMUNE MURINE CYTOTOXIC T LYMPHOCYTES INHIBIT CYTOTOXIC T-LYMPHOCYTE AND NATURAL KILLER ACTIVITY: STRAIN SPECIFICITY OF INHIBITION.

Lawlor DA, Saunders PH, Ware CF
Div. Urology, Univ. Texas Health Science Center, San Antonio, TX, 78284
Cell Immunol; 68(1):128-138 1982

Xenogeneic antisera directed against alloimmune murine peritoneal exudate lymphocytes (IPEL) inhibit, in the absence of complement, in vitro T-cell-mediated cytolysis by IPEL and, to a comparable degree, cytolysis by in vitro-sensitized splenic cytotoxic T lymphocytes. Since inhibition by rat antiserum directed against C57Bl/6J (B6) IPEL was obtained with alloimmune cytotoxic T lymphocytes (CTL) from several different inbred strains of divergent major histocompatibility complex (MHC) specificity, the inhibitory antibodies are not directed against idiotypic portions of the T-cell receptor. Moreover, antibodies directed against constant or variable Lyt 2,3 determinants appear not to be involved, since xenoantiserum-mediated inhibition of CTL is independent of effector cell Lyt 2,3 phenotype, and since absorption of the xenoantiserum with Lyt 2,3-positive cells failed to reduce either titer or strength of the inhibitory activity. In other studies we obtained strong inhibition, by the rat antiserum directed against IPEL, of natural killer (NK) cells. Our results support the presence on alloimmune CTL (derived by either in vivo or in vitro immunization) and NK effectors of lytic molecules or membrane components, independent of Lyt 2,3 entities. (Author abstract) (29 Refs)

### 27. THE CHARACTERIZATION AND FUNCTION OF HUMAN IMMUNOREGULATORY T LYMPHOCYTE SUBSETS.

Reinherz EL, Scholssman SF
Div. Tumor Immunology, Sidney Farber Cancer Inst., Boston, MA
Pharmacol Rev; 34(1):17-22 1982

Functional T lymphocyte subpopulations can be identified in humans by antibodies which detect stable glycoprotein antigens on their surface. Thus, inducer T lymphocytes bear an antigen termed T4 while suppressor T lymphocytes bear an antigen termed T5. Immune homeostasis results from a delicate balance between inducer and suppressor subsets within the T-cell circuit and perturbation in subset dynamics may initiate a wide variety of immunopathological disorders. The authors discuss the present understanding of this circuit, its role in the pathogenesis of a number of disease, and how the human immune response can be manipulated in an orderly way through modulation of selected T-cell subsets. (Author abstract) (55 Refs)

### 28. A HUMAN T-CELL ANTIGEN DEFINED BY XENOANTISERUM TO SEZARY LEUKEMIC CELLS: IMMUNOCHEMICAL AND FUNCTIONAL STUDIES.

Ogasawara M, Ishii Y, Kamiya H, Kikuchi K
Dept. Pathology, Sapporo Medical Coll., S1 W17 Sapporo 060, Japan
Am J Hematol; 12(2):95-107 1982

Xenoantiserum to Sezary cell leukemia cells (ASS) was developed by immunizing rabbits with those cells and was absorbed with human red cells, liver, tonsil B cells, and cultured Raji cells. This reagent reacted by immunofluorescence with virtually all human thymus and T cells. In the thymus, medullary cells reacted more strongly with ASS than did cortical thymocytes. When immunoprecipitates that formed between

ASS and 125I-labeled lymphocyte surface glycoproteins were analyzed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, it was found that ASS precipitated a 72K mol wt (MW) glycoprotein from T cells but not from B cells. On the other hand, it was shown by functional studies that T cells sensitive to the cytotoxic effect of ASS contained T cells that could aid the immunoglobulin synthesis of B cells induced by pokeweed mitogen. On the other hand, suppressor T cells induced by concanavalin A resided in those cells rather resistant to its cytotoxic effect. These data support the idea that the 72K MW glycoprotein on human thymus and T cells might be homologous to mouse Lyt-1 antigens. (Author abstract) (27 Refs)

### 29. T-LYMPHOCYTE RECONSTITUTION IN RECIPIENTS OF BONE MARROW TRANSPLANTS WITH AND WITHOUT GVHD: IMBALANCES OF T-CELL SUBPOPULATIONS HAVING UNIQUE REGULATORY AND COGNITIVE FUNCTIONS.

**Friedrich W, O'Reilly RJ, Koziner B, Gebhard DF, Good RA, Evans RL**
**(c/o Evans), Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021**
**Blood; 59(4):696-701 1982**

The development of T lymphocytes in 34 patients engrafted with allogeneic bone marrow was studied by indirect immunofluorescence using mouse monoclonal antibodies. Two antibodies, termed anti-Leu-1 and anti-Leu-4, react with distinct membrane components expressed by all peripheral T cells, whereas two other antibodies, termed anti-Leu-2a and anti-Leu-3a, react with complementary subsets of Leu-1+ and Leu-4+ lymphocytes. The Leu-2a+3a- (Leu-2) subset contains suppressor/cytotoxic T cells, and the Leu-2a-3a+ (Leu-3) subset contains helper T cells. The ratio of Leu-2/Leu-3 T cells was elevated in nearly all patients studied during the 1st mo of engraftment, but this ratio subsequently returned to normal in patients with an uncomplicated course or with solved acute GVHD. In contrast, a deficiency of helper T cells with a resultant preponderance of suppressor/cytotoxic T cells persisted in all patients studied with both acute and chronic GVHD after the 1st mo. The implications of these findings in regard to the functions of these cells in vitro are discussed. (Author abstract) (23 Refs)

### 30. EVIDENCE THAT ANTISERA THAT REACT WITH PRODUCTS OF THE HUMAN HLA-DR LOCUS MAY BLOCK IN VITRO ANTIGEN-INDUCED PROLIFERATION BY INDUCING SUPPRESSION.

**Muchmore AV, Decker JM, Mann DL**
**Metabolism Branch, NCI, NIH, Bethesda, MD, 20205**
**J Immunol; 128(5):2063-2066 1982**

It is widely recognized that antisera that interact with determinants encoded by the Ia region of the mouse and its counterpart, the DR locus of man, are capable of interfering with the ability of monocytes and lymphocytes to respond in vitro to an antigenic stimulus. Using an in vitro assay that measures antigen-specific proliferation of human lymphocytes, we found that both a heteroantiserum raised in rabbits (anti-P29,34) and alloantisera which recognize determinants encoded for by the human DR locus dramatically block in vitro antigen-specific proliferation. These anti-DR antisera appear to act at the level of the monocyte; monocytes pulsed and washed free of excess antisera fail to promote proliferation in the presence of soluble antigen and untreated T cells whereas identically pulsed and washed T cells respond normally with untreated monocytes. Furthermore, the addition of unpulsed monocytes fails to restore in vitro antigen-specific reactivity. Our data suggest that membrane-bound anti-DR-specific antisera on monocytes is profoundly suppressive, and also suggests simple steric hindrance may not account for all of the observed effects such antisera have on monocyte-T cell interactions. (Author abstract) (25 Refs)

### 31. GENETIC CONTROL OF CELL-CELL INTERACTIONS.

**Katz DH**
**Dept. Immunology, Medical Biology Inst., 11077 North Torrey Pines Road, La Jolla, CA, 92037**
**Pharmacol Rev; 34(1):51-62 1982**

Genetic restrictions on immunocompetent cell interactions, studies on adaptive differentiation of lymphocytes in bone marrow chimeras, orchestration of cooperating phenotypes of conventional F1 lymphocytes, and parallelisms between the cell interaction and immune response phenotypes are discussed. Recent studies bearing directly on the relationships between receptors involved in intercellular communication and the phenotype of cell-cell interactions ultimately displayed by a given lymphoid cell population are emphasized. (53 Refs)

### 32. STRUCTURAL HOMOLOGY OF A MACROPHAGE DIFFERENTIATION ANTIGEN AND AN ANTIGEN INVOLVED IN T-CELL-MEDIATED KILLING.

**Kurzinger K, Ho MK, Springer T**
**Lab. Membrane Immunochemistry, Sidney Farber Cancer Inst., Harvard Medical Sch., Boston, MA, 02115**
**Nature; 296(5858):668-670 1982**

The cellular distribution and molecular structure of two murine cell-surface antigens, macrophage differentiation antigen 1 (Mac-1) and lymphocyte-function-associated antigen 1 (LFA-1) were investigated. Mac-1 is expressed on macrophages, natural killer cells and 50% of bone marrow cells, but not on B or T lymphocytes. LFA-1 is expressed on B and T lymphocytes and 75% of bone marrow cells, but not on macrophages. Mac-1 and LFA-1, which share some common antigenic determinants recognized by monoclonal antibodies, comprise a novel family of leukocyte differentiation antigens. The two antigens have alpha-chains of mol wt 170,000 and 180,000, respectively; both have beta-chains of mol wt 95,000. Cross-linking studies indicate a non-covalent association of the subunits into an alpha-1-beta-1 quaternary structure. (11 Refs)

## CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION

### 33. MECHANISM OF T CELL ACTIVATION: ROLE AND FUNCTIONAL RELATIONSHIP OF HLA-DR ANTIGENS AND INTERLEUKINS.

**Palacios R**
**Dept. Immunobiology, Wallenberglaboratory, Karolinska Inst., Lilla Frescati, S-104 05 Stockholm 50, Sweden**
**Immunol Rev; 63:73-110 1982**

The mechanism by which non-activated T-lymphocytes become sensitive to interleukin 2 (IL2) is reviewed. T cells appear to be sensitized to IL 2 during activation by HLA-DR antigens by the induction of IL-2 receptors, which occurs when foreign antigen from antigen-presenting cells plus HLA-

DR molecules interact with the corresponding T cell receptors. Studies on the control of IL-2 synthesis are reviewed in various systems. (83 Refs)

### 34. THE BIOCHEMISTRY, BIOLOGY, AND ROLE OF INTERLEUKIN 2 IN THE INDUCTION OF CYTOTOXIC T CELL AND ANTIBODY-FORMING B CELL RESPONSES.

**Farrar JJ, Benjamin WR, Hilfiker ML, Howard M, Farrar WL, Fuller-Farrar J**
**Lab. Microbiology and Immunology, Natl. Inst. Dental Res., NIH, Building 30, Room 326, Bethesda, MD, 20205**
**Immunol Rev; 63:129-166 1982**

The use of phorbol esters to optimize the production of immunoenhancing lymphokines by spleen cells, peripheral blood WBC, and T cell lines is reported. Recent findings on the molecular structure of murine thymoma-derived interleukin 2 (IL2) and the interaction of the factor with its receptor are described. The separation and characterization of a group of other lymphokines which are biochemically and functionally distinct from IL2, but which exhibit similar biological effects in some non-discriminating bioassays, is reviewed. Evidence for the lymphokine cascade is presented. (87 Refs)

### 35. PHYSICOCHEMICAL SURFACE CHANGES ON PHAGOCYTIC CELLS DURING DIFFERENTIATION IN RELATION TO CHEMOTAXIS AND PHAGOCYTOSIS.

**Stendahl O, Dahlgren C, Hed J, Breton-Gorius J, Basford RE, Gallily R, Harkness RA**
**Dept. Medical Microbiology, Linkoping Univ. Medical Sch., S-581 85 Linkoping, Sweden**
**Adv Exp Med Biol; 141:531-537 1982**

Alterations in certain physicochemical surface properties and related functional differentiation were studied in the human promyelocytic leukemia cell line HL-60. HL-60 cells induced to differentiate in the presence of dimethylsulfoxide (DMSO) underwent a decrease in volume. Surface charges were assayed in aqueous two-polymer phase systems. Bis-trimethylamino ((CH3)3N+)-polyethyleneglycol (TMA-PEG) influenced the partition of undifferentiated, differentiated and the control polymorphonuclear leukocytes (PMNL) to the same extent. In contrast, both DMSO-treated HL-60 cells and mature granulocytes showed increased hydrophobic interaction with palmitoyl-PEG compared to immature HL-60 cells. When 3-6 day cultures of HL-60 cells in DMSO were tested for migration and chemotactic response, the DMSO-treated cells migrated and responded as well as control PMNL. The ingestion of IgG- and C3-opsonized yeast particles was assayed during differentiation. Within 2 days, the C3-dependent ingestion increased from less than 10% to 25%, whereas IgG-dependent ingestion increased more slowly. This difference in rates of ingestion may reflect formation of complement and IgG receptors at different rates. The data indicate that oxidative and phagocytic responsiveness are acquired at different stages of differentiation. (15 Refs)

### 36. LOSS OF TRANSFERRIN RECEPTORS FOLLOWING INDUCED DIFFERENTIATION OF HL-60 PROMYELOCYTIC LEUKEMIA CELLS.

**Yeh CJ, Papamichael M, Faulk WP**
**Blond McIndoe Centre for Transplantation Biology, Queen Victoria Hosp., East Grinstead, Sussex RH19 3DZ, England**
**Exp Cell Res; 138(2):429-433 1982**

Human promyelocytic leukemia (HL-60) and lymphoblastoid (Daudi) cells were studied for transferrin receptors before and after induced differentiation with dimethyl sulfoxide (DMSO), sodium butyrate or retinoic acid. None of these reagents affected the morphology or presentation of receptors in Daudi cells, but many HL-60 morphologically matured to banded neutrophils and demonstrated a concomitant loss of transferrin binding, suggesting an important role of transferrin receptors in cellular differentiation. (Author abstract) (31 Refs)

### 37. GENETIC ASPECTS OF MACROPHAGE ACTIVATION FOR TUMOR CYTOTOXICITY.

**Boraschi D**
**Istituto di Ricerche Farmacologiche 'Mario Negri', Milano, Italy**
**Adv Exp Med Biol; 141:119-128 1982**

Defective macrophage activation was studied in mouse strains A/J and P/J with low macrophage tumoricidal activity in comparison with strain C3H/HeN with high and C3H/HeJ with low activity. Cells from these strains were compared for their ability to respond to chemotactic stimuli, to phagocytize IgG-opsonized RBC, and to express the cytochemical marker peroxidase. Inflammatory events took place normally in A/J mice comparable to those in the control strains. P/J macrophages showed a profound abnormality in phagocytic capacity. P/J lymphocytes also showed a profound defect in macrophage activating lymphokine (MAF) activity. When P/J mice were tested for production of two other lymphokines, the chemotactic factor (LDCF) was normal whereas they were defective for production of immune interferon. Macrophages from P/J mice showed a difference in reactive mononuclear phagocytes in response to two activation stimuli. As in the other studies, the defects in the macrophages of C3H/HeJ and A/J mice were phenotypically similar while those of P/J mice were distinct. Macrophages of A/J and P/J were sensitive to lipopolysaccharide (LPS) toxicity in vitro in contrast to C3H/HeJ, indicating a genetic difference. By genetic analysis it was possible to demonstrate C3H/HeJ and A/J macrophage defects had a different genetic basis. Further studies with the use of backcross mice showed that the A/J tumoricidal defect is controlled by at least two genes. The lymphocyte proliferation defects in response to LPS appears to be under the control of a single gene. (22 Refs)

### 38. ANALYSIS OF ANTIGENIC DETERMINANTS ON HUMAN MONOCYTES AND MACROPHAGES.

**Todd RF, Schlossman SF**
**Div. Tumor Immunology, Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115**
**Blood; 59(4):775-786 1982**

Mo1, 2, 3, and 4, and Plt-1 are a series of five distinct antigens detected on the surface of human peripheral blood monocytes by mouse monoclonal antibodies. Mo2 and 3 are restricted to the monocyte-macrophage series, while Mo1, as previously reported, is also expressed by human granulocytes and null cells. Mo3, as distinguished from Mo1 and Mo2, is weakly expressed by virgin peripheral blood monocytes but becomes well expressed if monocytes are cultured overnight at 37 C. Mo4 is coexpressed by monocytes and platelets, while Plt-1 appears to be a platelet-specific antigen whose detection on monocytes reflects adherence of platelets to monocyte membranes. That Mo2-4 are true monocyte antigens is demonstrated by their resynthesis following protease treatment of monocytes (Mo1 expression is resistant to proteolytic digestion). During myeloid-monocyte differentiation, the Mo antigens are infrequently expressed by immature myeloid cells but are found at higher frequency on leukemic monocytic forms. Ma-

crophages from cultured peripheral blood monocytes and HL-60 cells exposed to lymphokines or phorbol diester express Mo1-4, but noncirculating peritoneal macrophages lack Mo3. the Mo antigens are differentiation markers whose expression reflects membrane heterogeneity during myeloid-monocyte-macrophage maturation. (Author abstract) (36 Refs)

### 39. MECHANISMS OF TARGET RECOGNITION AND DESTRUCTION IN MACROPHAGE-MEDIATED TUMOR CYTOTOXICITY.

**Adams DO, Johnson WJ, Marino PA**
**Dept. Pathology and Microbiology-Immunology, Duke Univ. Medical Center, Durham, NC, 27710**
**Fed Proc; 41(6):2212-2221 1982**

Macrophages can be activated to kill neoplastic cells selectively and efficiently. Recent studies from this laboratory on mechanisms of target recognition and injury operative in such lysis have centered on the binding of tumor targets to and the secretion of a cytolytic protease (cytolytic factor [CF]) by activated murine macrophages. Activated macrophages selectively and extensively bind neoplastic cells; nonselective binding of a low degree is seen between numerous other cell pairs. The selective binding of three nonadherent tumors, which is much firmer than the nonselective binding, appears to depend on shared recognition structures contained within plasma membranes of the three tumors. Activated macrophages also secrete a potent, cytolytic, serine protease of mol wt approx 40,0000. Secretion of CF is closely correlated with activation for cytolysis, and specific protease inhibitors of CF block macrophage-mediated cytotoxicity. Binding of tumor cells to activated macrophages triggers augmented secretion of CF. Several lines of evidence indicate that the capacity for selective binding and the capacity for secreting CF are separate and independently regulated functions of activated macrophages and that each is necessary but not sufficient for completion of macrophage-mediated tumor cytotoxicity. Analysis of the complete lytic interaction between activated macrophages and tumor cells suggests that binding and then secretion of CF are sequentially involved. These data have been integrated into a minimal hypothetical model, which suggests that macrophage-mediated tumor cytotoxicity is a multistep event encompassing (1) selective binding of tumor cells to the surface of activated macrophages and (2) secretion of multiple lytic effector substances, including CF, from the activated macrophages. (Author abstract) (35 Refs)

### 40. DIFFERENTIATION OF HUMAN T LYMPHOCYTES: II. PHENOTYPIC DIFFERENCE IN SKIN AND BLOOD MALIGNANT T-CELLS IN CUTANEOUS T-CELL LYMPHOMA.

**Haynes BF, Hensley LL, Jegasothy BV**
**Dept. Medicine, Duke Univ. Medical Center, Box 3258, Durham, NC, 27710**
**J Invest Dermatol; 78(4):323-326 1982**

The cell surface antigen phenotype of circulating and skin malignant T-cells in patients with cutaneous T-cell lymphoma were studied. The mature T-cell antigen phenotype of the malignant T-cells was identical for circulating and skin malignant T-cells. In contrast, skin malignant T-cells expressed the immature human T-cell antigen Thy-1, surface membrane transferrin receptors, and Ia-like determinants while circulating malignant T-cells did not express these antigens. Skin infiltrating T-cells in benign dermatoses also expressed Thy-1 and Ia-like determinants. These observations support the notion that the skin is a major site of extrathymic T-cell differentiation and may promote phenotypic changes in circulating T-cells that home to skin. (Author abstract) (24 Refs)

### 41. CHARACTERIZATION OF FIVE CLONED MURINE CELL LINES SHOWING HIGH CYTOLYTIC ACTIVITY AGAINST YAC-1 CELLS.

**Brooks CG, Kuribayashi K, Sale GE, Henney CS**
**Program in Basic Immunology, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104**
**J Immunol; 128(5):2326-2335 1982**

In an attempt to provide a selection procedure for the long-term growth and subsequent cloning of NK cells, mouse lymphocytes were treated with monoclonal anti-Thy-1.2 antibody and complement, incubated for 24 hr with poly I:C to boost residual NK cell activity, and then transferred into growth medium containing supernatant from Con A-stimulated mouse spleen cells. After cloning on appropriate feeder cells, two clones of C57BL/6 origin and three CBA clones were isolated and studied in detail. All five clones had several features in common with splenic NK cells. Morphologically, the cells were large and contained prominent azurophilic granules. Although YAC-1 cells were the most sensitive target cells for the cloned lines, all the clones showed cytolytic reactivity somewhat different from that of normal or activated splenic NK cells. In particular, cytotoxicity by one clone, tested on a panel of 44 target cells, was generally restricted to murine lymphoid tumor target cells. With this cytotoxic clone there was, most strikingly, an almost complete lack of cytotoxicity against either solid-tumor-derived targets or against xenogeneic targets. Of major interest was the observation that two of the cloned cell lines bore high quantities of Lyt-2 antigen, whereas the other three lines had very small or undetectable (by flow cytofluorimetry) amounts of this antigen. In other respects (specificity, surface markers, cytochemistry), the Lyt-2-positive and Lyt-2-negative cell lines were extremely similar. The existence of two cloned cell lines expressing simultaneously characteristics of both NK cells and cytotoxic T lymphocytes is intriguing and suggests the possibility of a close relationship between these two lineages of cells. (71 Refs)

### 42. STUDIES ON CHRONIC MYELOID LEUKEMIA CELL POPULATIONS WITH COLONY-FORMING ABILITIES IN PHA-LEUKOCYTE FEEDER AND ROBINSON ASSAYS.

**Swart K, Hagemeijer A, Lowenberg B**
**(c/o Lowenberg) Inst. Hematology, Erasmus Univ., P.O. Box 1738, 3000 DR Rotterdam, The Netherlands**
**Leuk Res; 6(1):55-62 1982**

Growth of chronic myeloid leukemia cells in phytohemagglutinin-leukocyte feeder (PHA-lf) and Robinson assays was compared after removal of T lymphocyte precursors by erythrocyte-rosette formation and fractionation on discontinuous albumin gradients. In PHA-lf tests, cells in the 1.056 and 1.059 g/ml density fractions grew pure leukemic colonies, while those from the 1.062 g/ml fraction grew mostly leukemic colonies. Recoveries with the Robinson technique were approximately the same for the two lighter fractions, but were smaller for the heaviest fraction, indicating that the two techniques separated different subpopulations. In addition, the Robinson colony cells showed some differentiation, while those from the PHA-lf assay were almost entirely blast-type cells. Dissimilarities between the two assays were most apparent with cells from patients in blast crisis. The PHA-lf technique may given useful additional information about cell subpopulations to supplement the standard tests. (13 Refs)

### 43. GENETIC ANALYSIS OF THE ROLE OF CAMP IN MEDIATING EFFECTS OF INTERFERON.

Schneck J, Rager-Zisman B, Rosen OM, Bloom BR

Dept. Microbiology and Immunology, Albert Einstein Coll. Medicine, Bronx, NY, 10461

Proc Natl Acad Sci USA; 79(6,part1):1879-1883 1982

The effects of interferon (IFN) on Fc receptor-mediated phagocytosis, intracellular cAMP levels, antiviral activity, and growth inhibition were analyzed in a cloned macrophage-like cell line, J774.2, and variants derived from it. Purified IFN increased Fc receptor-mediated phagocytosis in J774.2 cells, and in cAMP-responsive nonphagocytic variants but was without effect in cAMP-unresponsive nonphagocytic variants, in adenylate cyclase-deficient variants, and in cAMP-dependent protein kinase-deficient variants. Under conditions in which IFN augmented phagocytosis, it increased intracellular levels of cAMP. Parental cells were highly sensitive to IFN-mediated growth inhibition. In contrast, cAMP-dependent protein kinase-deficient variants were only 1/100th as sensitive to growth inhibition by IFN. All cell lines tested, both responsive and unresponsive to cAMP, were equally protected by IFN against infection with vesicular stomatitis virus, demonstrating that the antiviral state was independent of cAMP. These results indicate that, in transformed macrophages, stimulation of phagocytosis and inhibition of growth by IFN are mediated through intracellular cAMP, whereas the antiviral state induced by IFN is independent of cAMP. (Author abstract) (31 Refs)

## EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS

### 44. TUMOR PROMOTER 12-O-TETRADECANOYLPHORBOL 13-ACETATE: EFFECT ON COMPLEMENT AND EPSTEIN-BARR VIRUS RECEPTORS IN HUMAN LYMPHOBLASTOID CELL LINES.

Yamamoto N, Mitsuma T, Vogt A

(c/o Vogt) Institut fur Immunologie, Zentrum fur Hygiene, Universitat Freiburg, Hermann-Herder-Str. 11, 7800 Freiburg, W. Germany

JNCI; 68(3):385-390 1982

The effect of the tumor promoter 12-O-tetradecanoylphorbol 13-acetate (TPA) on the C3 and Epstein-Barr virus (EBV) receptors in various human lymphoblastoid cells was investigated with the use of the erythrocyte-antibody-complement (EAC) rosette formation method and a quantitative bioassay for EBV receptors. TPA caused a significant decrease of C3 receptors in the cultures of both Raji and SB4 cells (by approximately 50% of the C3 receptors in untreated cultures at 10 ng/ml). Kinetic studies revealed that the rate of reduction was rather moderate but progressive, reaching a maximum 5 days after treatment with TPA. Kinetic studies showed that EBV receptors also decreased, similar to the reduction seen with C3 receptors after TPA treatment. The effect of TPA on the reduction of C3 receptors was observed not only in these cells but also in other EBV-positive B-cells, subclones of SB4 cells, and MOLT-4 cells. However, in an EBV-negative B-cell line, BJAB, EAC rosette formation was significantly enhanced. (Author abstract) (38 Refs)

### 45. NON-GLUCOCORTICOID RECEPTOR-MEDIATED EFFECTS OF THE POTENT GLUCOCORTICOID DEACYLCORTIVAZOL.

Harmon JM, Schmidt TJ, Thompson EB

Lab. Biochemistry, Div. Cancer Biology and Diagnosis, NCI, NIH, Bethesda, MD, 20205

Cancer Res; 42(6):2110-2114 1982

Deacylcortivazol (DAC), a potent glucocorticoid, contains a phenyl-pyrazole moiety fused to the 2-3 positions of the traditional steroid nucleus. When incubated with glucocorticoid-resistant mutants derived from the glucocorticoid-sensitive human leukemic cell line CEM-C7, DAC caused significant growth inhibition. However, this effect required 1 uM DAC, a concentration 50 times higher than that necessary for glucocorticoid receptor saturation. Cytotoxicity was observed in both mutants containing high-affinity glucocorticoid receptors defective in nuclear translocation and a mutant completely devoid of receptors. Further, in dexamethasone-resistant clones, DAC elicited only marginal increases in the activity of the glucocorticoid-inducible enzyme glutamine synthetase. Clones resistant to high concentrations of DAC could not be directly isolated from CEM-C7. However, stable DAC-resistant clones could be isolated from dexamethasone-resistant subclones of CEM-C7 with a frequency of 1 to 8 x 10(-4). These data are consistent with resistance to DAC being acquired in a two-step process. Our results suggest that the cytotoxicity of DAC at concentrations higher than necessary for glucocorticoid receptor saturation is not mediated by glucocorticoid receptors. Thus, DAC may be a bifunctional compound having both steroid receptor-mediated and receptor-independent cytotoxicity. (Author abstract) (28 Refs)

### 46. CIMETIDINE AND THERAPY OF RODENT TUMOURS.

Hannant D, James K, Bolton RE, Robertson MD, Milne I

Medical Branch, Inst. Occupational Medicine, Roxburgh Place, Edinburgh EH8 9SU, Scotland

Br J Cancer; 45(4):613-614 1982

Effects of cimetidine (CM: 100 mg/kg/day for 29-38 days) on tumor growth were studied in male syngeneic WAG/Ed rats inoculated sc with 10(5) asbestos-induced mesothelioma MF3 cells and in syngeneic CBA/Ca mice inoculated with 10(5)-10(6) methylcholanthrene-induced fibrosarcoma CCH1 cells. Spleen cells were prepared from syngeneic WAG/Ed rats and the effect of CM on in vitro binding of histamine to spleen lymphocytes was examined. CM had no observable effect on the incidence or size of tumor in the rat and mouse models. The ability of CM to produce a response in the CCH1 sarcoma in a different mouse strain is discussed. Lack of CM effect in the rat mesothelioma did not result from absence of H-2 antagonist activity. In vitro studies showed that histamine was able to bind specifically to 33.9% of normal WAG/Ed rat spleen cells. Pretreatment of the cells with 10(-3) M CM for 1 hr at 37 C reduced the fluorescent staining to 12.1%. Thus, although CM failed to influence tumor growth, it did bind in vitro to H-2 receptors on rat spleen cells. (8 Refs)

## OTHER RELATED STUDIES

### 47. NEWER METHODS OF CANCER TREATMENT: SECTION 1. IMMUNOTHERAPY.

Terry WD, Hodes RJ
Immunology Branch, NCI, Bethesda, MD
Cancer - Principles and Practice of Oncology. DeVita VT, Hellman S, and Rosenberg SA, ed. Philadelphia, Lippincott, 1926 pp., 1982.

Discussions relative to immunotherapy center around history, therapeutic agents, clinical trials, and conclusions. Immunotherapy is still in the early stages of development as a cancer treatment. A few facts seem to be established: that the development of delayed hypersensitivity reactions in a tumor leads to tumor necrosis; that id or iv BCG administration slightly prolongs remissions and causes a somewhat longer prolongation of post-relapse survival time in patients with acute myelogenous leukemia; that BCG treatment reduces the frequency of recurrences of papillary carcinoma of the bladder; and that levamisole may be a useful treatment for several types of cancer. The slow progress of clinical immunotherapy is related to the very large number of potential variables in the host-tumor-therapy interaction, which in turn has meant that the development of immunotherapy remains empirical. Additional information on the surface antigens of tumor cells, immune system-tumor cell interactions, and the regulation and control of immunologic function must be obtained before rational decisions can be made on the basis of the probability that immunotherapy will be useful in the systemic treatment of cancer. (235 Refs)

### 48. SYSTEMIC ADMINISTRATION OF HUMAN LEUKOCYTE INTERFERON TO MELANOMA PATIENTS. I. EFFECTS ON NATURAL KILLER FUNCTION AND CELL POPULATIONS.

Golub SH, Dorey F, Hara D, Morton DL, Burk MW
Div. Oncology, Dept. Surgery, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA, 90024
JNCI; 68(5):703-710 1982

Natural killer (NK) cytotoxicty was assessed against K562 targets in 14 melanoma patients who received daily im doses of human leukocyte interferon (IFN) for 42 consecutive days. The most common pattern of NK activity was a decline from pretreatment levels 1 day after initiation of treatment, followed by increasing cytotoxicity with peak activity at Day 7 and a subsequent gradual decline to pretreatment levels during the remaining wk of treatment. This pattern was particularly apparent in patients who received 3 x 10(6) or 9 x 10(6) U IFN/day, while patients who received 1 x 10(6) U IFN/day tended to lack the decline at Day 1 and maintained the elevated NK activity past Day 7. Changes in NK activity could not be related to changes in absolute lymphocyte counts; to proportions of cells bearing membrane receptors for sheep RBC, of cells bearing membrane receptors for erythrocyte-antibody-complement, or of cells bearing FCgamma receptor, or to clinical response to IFN. (Author abstract) (23 Refs)

### 49. OBJECTIVE REGRESSIONS OF T- AND B-CELL LYMPHOMAS IN PATIENTS FOLLOWING TREATMENT WITH ANTI-THYMOCYTE GLOBULIN.

Fisher RI, Silver BA, Vanhaelen CP, Jaffe ES, Cossman J
NIH, NCI, Building 10, Room 12N226, 9000 Rockville Pike, Bethesda, MD, 20205
Cancer Res; 42(6):2465-2469 1982

We have conducted a clinical trial utilizing anti-thymocyte globulin (ATG) for the treatment of patients with non-Hodgkin's lymphomas. Six patients were treated; 50% reductions in tumor mass of short duration were observed in one patient with a T-cell lymphoma and two patients with B-cell lymphomas. In vitro assays have been performed in an attempt to study the reactivity and potential mechanisms of antitumor action of the ATG. The ATG bound to essentially all normal blood mononuclear leukocytes as well as tumor cells from patients with T-, B-, or null cell lymphomas demonstrating its lack of specificity. Furthermore, complement-mediated lysis of normal mononuclear leukocytes, normal T- or B-cells, and tumor cells from two unresponsive patients were all comparable; moreover, since this lysis occurred only at concentrations of ATG that are not attainable in vivo, it is unlikely that complement-mediated cytotoxicity accounts for the responses observed. Peripheral blood lymphocyte counts and total erythrocyte rosettes did decrease during ATG treatment. Thus, objective tumor responses in both B- and T-cell non-Hodgkin's lymphomas can be achieved with a very nonspecific antiserum although significant toxicity resulted. Whether the magnitude or duration of response can be increased with monoclonal antibodies remains to be determined. Future success with serotherapy might require use of either a battery of different monoclonal antibodies or a single monoclonal antibody that can deliver radioisotopes, chemotherapy, or toxins to the tumor cells. (Author abstract) (13 Refs)

### 50. NATURAL KILLER CELL ACTIVITY IN GASTROINTESTINAL CANCER PATIENTS - DECLINE IN NATURAL KILLER CELL ACTIVITY IN TGAMMA CELLS AND THE ACTION OF INTERFERON ON ITS INCREASE.

Mugitani H, Suzuki M, Naruki Y, Ohtsuka S, Shinbo T
First Dept. Internal Medicine, Toho Univ. Sch. Medicine, Ota-ku, Tokyo, Japan
Nippon Gan Chiryo Gakkai Shi; 16(7):1371-1376 1981

Effects of interferon (IF) on natural killer (NK) cell activity of Tgamma-cells (IgG-Fc receptor-positive T cells) were investigated in peripheral blood lymphocytes of 21 patients with gastrointestinal cancer (17 gastric, 2 esophageal, 1 large intestine, and 1 gall bladder). T cells were isolated from peripheral blood lymphocytes, using the E-rosette sedimentation reaction; Tgamma-cells were isolated using theophylline. Release of 51Cr from 51Cr-labeled K562 cells was used to measure the NK cell activity. In 10 healthy subjects, the NK cell activity of mononucleocytes (MNC) was 46.5 +-13.1% and that of Tgamma-rich cells was 47.7 +-11.3%; these values were used as standards for NK cell activity in determinations of cytotoxic index. The cytotoxic index was applied to the NK cell activities of lymphocytes of the patients. The Tgamma cells showed a decline in NK cell activity in most of the 21 patients; there was also a decrease in NK cell activity in the MNC in these patients. Addition of 1,000 units of IF increased the NK cell activity of the MNC, T-rich and Tgamma-rich cells. The results suggested that the decreased NK cell activities of the Tgamma cells and the MNC may be due to decreased effector cell functioning and decreased production of IF. (27 Refs) (In JPN)

## 51. HUMAN NATURAL KILLER-LIKE ACTIVITY AGAINST MOUSE SPLEEN CELLS.

Yamamoto JK, Bialock JE, Johnson HM
(c/o Johnson) Dept. Microbiology, Univ. Texas Medical Branch, Galveston, TX, 77550
Eur J Immunol; 12(3):222-227 1982

Unstimulated human peripheral lymphocytes were cytotoxic for normal mouse spleen cells and suppressed the in vitro antibody plaque-forming cell (PFC) response of these cells to sheep red blood cells and dinitrophenylated Ficoll. The cells in the lymphocyte population that were responsible for the immunosuppression had properties of natural killer (NK) or NK-like cells in that they were: (a) non-E-rosetting, (b) nonadherent, (c) unaffected by treatment with anti-human immunoglobulin plus complement, (d) cytotoxic against an established human NK target, K562 leukemic cells, and (e) partially inactivated by mitomycin C. Addition of the human NK-like cells to mouse spleen cell cultures at the time of antigen addition and at an effector cell to target cell ratio as low as 0.67:1 resulted in 85 to 96% suppression of the PFC response. Addition of NK-like cells to cultures 18 hr before harvesting in 5-day cultures required higher concentrations and ratios (2.7:1) of effector to target cells to significantly suppress the PFC response. The data suggest that human NK-like activity in suppression of the mouse PFC response is due to killing of the targets. The mouse spleen cell PFC system represents a potential model for assessment of human NK activity that is quite dramatic in its effect and can be used in addition to the well known 51Cr-release assay. Also, since the mouse spleen cell is a normal cell, it provides a model in the PFC system for studying the mechanism of NK regulation of normal cellular function. An additional finding of this study was the observation that E-rosetting T cells significantly enhanced the mouse PFC response. Thus, human peripheral lymphocytes contain discrete cellular populations that either enhance or suppress the mouse PFC response. (Author abstract) (19 Refs)

## 52. T LYMPHOCYTE-MEDIATED SUPPRESSION OF MYELOMA FUNCTION IN VITRO. IV. GENERATION OF EFFECTOR SUPPRESSOR CELLS SPECIFIC FOR MYELOMA IDIOTYPES.

Abbas AK, Takaoki M, Greene MI
Dept. Pathology, Harvard Medical Sch., Boston, MA, 02115
J Exp Med; 155(4):1216-1221 1982

BALB/c mice were injected iv with viable syngeneic splenocytes to which affinity-purified M315 IgA was coupled developed suppressor T cells (Ts1) that inhibited IgA plaque-forming cells (PFC) after greater than 2 days in culture. On the other hand, T cells induced by soluble extracts of Ts1 cells (TsF1) and sc immunization suppressed greater than 50% of the PFC within 1 day and 80-90% by day 4. The cells mediating rapid suppression were operationally termed effector Ts. The specificity of the effector Ts was assessed by their ability to bind to different myeloma proteins. Suppressive activity was depleted by absorbing effector Ts on dishes coated with M315 IgA but not on dishes coated with MPC11 (IgG2b,k of unknown specificity) or M460 proteins. M315-specific effector Ts did not inhibit MPC 11 cells and caused greater than 70% selective suppression of IgA secretion by the MOPC 315-MPC11 somatic cell hybrid. Effector Ts were Thy-1.2+, Lyt-1-2+ cells, while Ts1 were either Lyt-1+2+ or T lymphocytes bearing both Lyt-1+ and Lyt-2+ markers were necessary for Ts1 to induce or mature into effector Ts in vitro. The ability to induce two cell types at different stages of a suppressor pathway, and to measure their effects on a monoclonal, autonomous target, should facilitate analysis of the differentiation and mechanisms of action of suppressor T lymphocytes. (11 Refs)

## 53. CORRELATED ANALYSIS OF CELLULAR DNA, MEMBRANE ANTIGENS AND LIGHT SCATTER OF HUMAN LYMPHOID CELLS.

Braylan RC, Benson NA, Nourse V, Kruth HS
Dept. Pathology, Univ. Florida Coll. Medicine, Gainesville, FL
Cytometry; 2(5):337-343 1982

Surface immunoglobulins (Ig), light scatter, and DNA of WIC and WAL cells (B-cell lymphoma lines bearing lambda-Ig and kappa-Ig, respectively) and of JM cells (a human T-cell line) stained with fluorescein (FITC)-labeled antibody, and propidium iodide (PI) were analyzed. Effects of ethanol fixation, ribonuclease (RNase) treatment, and PI staining of FITC emission were investigated. No differences were observed in green fluorescence emission of the unfixed, ethanol-fixed (EF), and PI-stained cells in any of the cell lines. EF cells retained surface Ig staining for more than 15 wk at 4 C. FITC fluorescence distributions of WIC and JM cells were unchanged. Effect of FITC staining on PI staining and emission was investigated. The DNA distributions were superimposable. Comparison of the distributions of surface membrane Ig and the T-cell antigens in the various phases of the cell cycle demonstrated in all cases a progressive increase in mean FITC fluorescence from G1 through S to G2-M. Mixtures of equal numbers of B- and T-cells were stained with either anti-light chain, or anti-Leu-1 antibodies, fixed, RNase-treated, and stained with PI. The DNA distributions obtained were superimposable on those obtained from each cell line separately. When effects of EF, RNase treatment, and PI staining on light scatter were analyzed, both B- and T-cell lines showed a decrease in the light scatter emission after 50% EF. After fixation, no differences in light scatter distributions were found between unstained and RNase treated, PI-stained cells. (20 Refs)

## 54. TG CELL INVOLVEMENT IN THE LEUKOCYTE ADHERENCE INHIBITION PHENOMENON.

Taylor SG, Saffold PC, Braun DP, Harris JE
Section Medical Oncology, Dept. Internal Medicine, Rush-Presbyterian-St. Luke's Medical Center, 1725 West Harrison St., Chicago, IL, 60612
JNCI; 68(4):549-554 1982

Peripheral blood mononuclear cells (PBMC), T-cells, non-T-cells, TG cells, and TM cells were tested for leukocyte adherence inhibition (LAI) reactivity to purified protein derivative (PPD) in normal human volunteers to determine the reactive cell subfractions. T-cells were separated by sheep red blood cell rosetting and TM and TG cells by rosetting with anti-ox red blood cell (ORBC) IgM- and IgG-treated ORBC. Fresh PBMC, T-cells, and TG cells gave positive LAI reactivity to PPD in PPD-positive donors only. PBMC that had undergone 24-hr incubation or extensive washing, non-T-cells, and TM cells were unreactive. All cell subfractions were negative in PPD-negative donors. Indirect LAI assay was performed on the spent media from overnight incubation of unstimulated PBMC and also following a 1-hr incubation of the various cell subfractions obtained from a PPD-reactive donor with PPD. Positive reactions, indicating the release of an LAI factor (LAIF), were obtained with the spent media and with the T-cell and TG cell subfractions following PPD stimulation, whereas non-T-cell and TM cell subfractions yielded no reactivity. Incubation of sensitized T-cells with PPD in the presence of cycloheximide and preincubation of T-cells for 24 hr

with cycloheximide before PPD exposure failed to inhibit LAI reactivity. These data suggest that T-cells, specifically TG cells, can release LAIF upon specific antigen stimulation with PPD, whereas non-T-cell and TM cell subpopulations fail to respond to the same stimulus. LAIF may also be released into the culture media with prolonged (overnight) incubation in artificial media or with extensive washing. Inhibition of protein synthesis during antigen exposure or up to 24 hr before antigen exposure does not appear to inhibit LAI reactivity. (Author abstract) (27 Refs)

### 55. MACROPHAGE ORIGIN OF REED-STERNBERG CELLS: AN IMMUNOHISTOCHEMICAL STUDY.

Payne SV, Wright DH, Jones KJ, Judd MA
(c/o Wright) Dept. Pathology, Southampton General Hosp., Level E, South Pathology Block, Southampton S09 4XY, England
J Clin Pathol; 35(2):159-166 1982

In an immunohistochemical study of 26 biopsies from 24 patients with Hodgkin's disease a granular staining pattern for alpha-1-antitrypsin (alpha1AT) and alpha-1-antichymotrypsin (alpha1ACT) was seen in Reed-Sternberg (RS) cells and mononuclear Hodgkin's (H) cells in over half the cases. The pattern of staining for these antiproteases seen in RS and H cells has previously only been observed in normal and malignant cells of the monocyte/macrophage lineage within the lymphoreticular system. A faintly granular evenly distributed staining for IgG was found in viable RS and H cells. This staining was associated with a similar distribution of both light chains but not J chain, suggesting that the immunoglobulin had not been synthesized by these cells but had been taken up from the extracellular environment. It is suggested that this uptake is an active process occurring in viable RS and H cells, possibly via Fcgamma receptors and further supports an origin from cells of the monocyte/macrophage lineage. IgA, IgD, albumin, fibrinogen, C1q, C4 and C3 were present in some cells, IgM was more rarely found and lysozyme was absent. The fact that cells staining for these serum proteins generally showed signs of degeneration and that the extent of staining correlated with the mol wt, but not serum concentration, of the protein suggests that they are passively acquired by dead or dying cells and thus represent a separate phenomenon from IgG uptake. The function of IgG uptake and accumulation by RS cells and the alpha1AT and alpha1ACT markers may prove of use in identifying the macrophage subtype from which these cells are derived. (Author abstract) (39 Refs)

### 56. ENUMERATION OF IL 2-SECRETING HELPER T CELLS BY LIMITING DILUTION ANALYSIS, AND DEMONSTRATION OF UNEXPECTEDLY HIGH LEVELS OF IL 2 PRODUCTION PER RESPONDING CELL.

Miller RA, Stutman O
Cellular Immunology Section, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
J Immunol; 128(5):2258-2264 1982

We describe here a method for estimating the frequency of alloantigen-responsive precursors of interleukin 2-(IL 2) secreting mouse T helper cells in spleen cell populations, and for measuring the amount of IL 2 generated by the progeny of each responsive cell over a 5-day culture period. Depending on the particular stimulus, about 1 T cell in every 30 to 300 can generate detectable levels of IL 2. Mis-locus incompatibilities activate a higher fraction of cells than do differences at the H-2 complex. The responder cell is sensitive to anti-Thy-1.2 antibody and complement, and is highly enriched in Lyt-2-populations as compared to positively selected Lyt-2+ cells. The dilution curve obtained is consistent with the idea that IL 2 production depends on a single class of T cell. The amount of IL 2 produced in these limiting dilution cultures is unexpectedly high: about 30-fold greater than the levels predicted by extrapolation from conventional mixed lymphocyte cultures. These results suggest that conventional cultures may be very responsive to regulatory events that do not occur at very low responder cell concentrations. Thus, limiting dilution analyses will provide insights into the effects of drugs, age, subset manipulation, etc, on the IL 2-producing cell itself, information that cannot be provided by conventional methods alone. (Author abstract) (34 Refs)

### 57. CELL LINEAGES IN HEMATOPOIETIC NEOPLASIA STUDIED WITH GLUCOSE-6-PHOSPHATE DEHYDROGENASE CELL MARKERS.

Fialkow PJ
Dept. Medicine, Univ. Washington, Seattle, WA, 98195
J Cell Physiol; Suppl1:37-43 1982

The indirect method based upon study of hematologic neoplasms arising in females whose X-chromosomes inactivation mosaicism is delineated with glucose-6-phosphate dehydrogenase (G6PD) markers is reviewed. Chronic myelogenous leukemia (CML), lymphocytes in CML, significance of Philadelphia chromosome (Ph), agnogenic myeloid metaplasia with myelofibrosis, other myeloproliferative disorders, acute nonlymphocytic leukemia (ANLL), chronic lymphocytic leukemia, applications of the G6PD system to the study of hematologic cell regulation in neoplasia, and potential applications of the G6PD system to the study of long-term hematologic cell cultures are discussed. Several types of investigations indicate that cells of CML clone differentiate into B-lymphocytes. The G6PD findings in lymphocytes in patients with CML indicate the existence of similar stem cells to those in rodents and that CML involves a stem cell pluripotent for lymphocytes as well as for myelogenous cells. Studies of G6PD and chromosomes in B-lymphoblastoid cell lines established from a patient with Ph-positive leukemia who was heterozygous for G6PD provide evidence for the existence of cells derived from the abnormal clone that are Ph-negative. Thus, acquisition of Ph may not be sufficient cause for the disease. Eight G6PD heterozygotes with ANLL have been studied. Only a single-enzyme G6PD phenotype was found in the leukemic blast cells, suggesting that the disorders in these patients were clonal. In the patients who were studied when their disease entered remission, a return to normal double-enzyme phenotype in granulocytic cells was observed. (47 Refs)

### 58. USE OF COVALENTLY BOUND ADJUVANT PEPTIDE TO INCREASE TUMOR IMMUNOGENICITY.

Eggers AE, Tarmin L, Ginsburg S
Columbia Univ., Coll. Physicians and Surgeons, 630 West 168th St., New York City, NY, 10032
Cancer Immunol Immunother; 12(2):167-172 1982

The active principle of Freund's complete adjuvant, N-acetyl-L-alanyl-D-isoglutamine (AP) was attached covalently through a spacer to the surface of poorly antigenic methylcholanthrene-induced sarcoma cells (MC-1) to stimulate in vitro and in vivo induction of direct cell-mediated cytotoxicity against tumor-associated antigens. The D-alanyl isomer of AP was non-stimulatory unless bound covalently to tumor cell surfaces. AP-coated spleen cells did not induce anti-MC-1 cytotoxicity. Attaching AP directly to MC-1 cells was more effective than attaching it to neutral accessory spleen cells. Spleno-

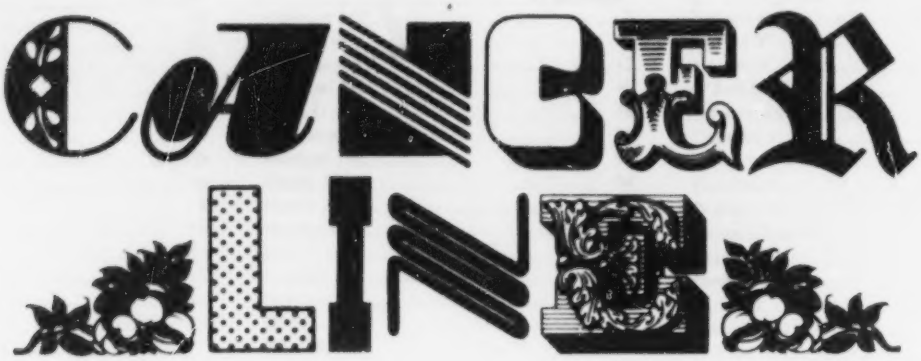
cytes sensitized in vitro against AP-treated MC-1 cells were shown to cross react with 3152 cells (a non-H2-matched methylcholanthrene-induced fibrosarcoma) and B6 tail epidermal cells, but not with EL4 cells (a B6 lymphoma) or B6 splenocytes. Nude mice did not develop cytotoxicity against AP-coated MC-1 cells, whereas heterozygous littermates and beige mice did. The results suggested that the effector cells are T cells with a broad pattern of reactivity. In vivo immunization with MC-1 cells coated with spacer and AP was found to elicit anti-tumor cytotoxicity that could be increased by pretreating mice with cyclophosphamide in doses known to ablate suppressor cells. The max cytotoxicity seen was 36.2%. Attempts at treating mice with progressively growing MC-1 tumors with MC-1-spacer-AP 'vaccine' showed a therapeutic effect with small tumors but not with large tumors. (16 Refs)

U.S. GOVERNMENT PRINTING OFFICE: 1992—[illegible]

# AUTHOR INDEX WITH CITATION NUMBERS


Abbas AK 52
Adams DO 39
Aisenberg AC 5
Anderson VA 13
Askonas BA 20
Astaldi A 16
Basford RE 35
Benjamin WR 34
Benson NA 53
Blalock JE 51
Bloom BR 43
Bohn B 10
Bolton RE 46
Boltz-Nitulescu 15
Bonnard GD 7
Boraschi D 37
Bowman WP 2
Braun DP 54
Braylan RC 53
Breton-Gorius J 35
Brooks CG 41
Burk MW 48
Butcher EC 22
Campbell MA 6
Capel PJ 25
Carboneil A 9
Chazot G 8
Chiao JW 18
Cosman J 49
Dahlgren C 35
Dailey MO 22
De Groot J 25
De Waal RM 25
Decker JM 30
Devlin JJ 23
Dolan MF 7
Dorey F 48
Dorken B 10
Dow LW 2
Eggers AE 58
Evans RL 29
Fanger MW 17
Farrar JJ 34
Farrar WL 34
Fathman CG 22
Fauci AS 7
Faulk WP 36
Fialkow PJ 57
Fisher RI 49
Frade R 19
Friedrich W 29
Fu SM 24
Fuller-Farrar J 34
Gallily R 35
Gathings WE 24
Gebhard DF 29
Ginsburg S 58
Golub SH 48
Good RA 29
Gordon J 13
Gourdin MF 14
Gramatzki M 7
Granger GA 23
Greaves MF 1
Greene MI 52
Hagemeijer A 42
Hannant D 46
Hara D 48
Harkness RA 35
Harmon JM 45
Harris JE 54
Harris NL 5
Haynes BF 40
Hed J 35
Henney CS 41
Hensley LL 40
Hilfiker ML 34
Ho MK 32
Hodes RJ 47
Holden CA 6
Howard M 34
Hunstein W 10
Ishii Y 28
Jaffe ES 49
James K 46
Jegasothy BV 40
Jeijlemaker WP 16
Johnson HM 51
Johnson WJ 39
Jones KJ 55
Judd MA 55
Kamiya H 33
Katz DH 31
Kibbelaar MD 25
Kikuchi K 28
Kincade PW 24
Kipp DE 20
Knight KL 17
Koene RA 25
Koh HK 5
Koziner B 29
Kruth HS 53
Kuribayashi K 41
Kurzinger K 32
Kusakari A 3
Landreth KS 24
Laurent G 14
Lawlor DA 26
Lee G 24
Look AT 2
Lowenberg B 42
MacDonald DM 6
MacKenzie MR 9
Mann DL 30
Maples JA 7
Marino PA 39
Mauer AM 2
Melief CJ 16
Miller CH 9
Miller RA 56
Milne I 46
Mirchandani I 4
Mitsuma T 44
Morton DL 48
Muchmore AV 30
Mugitani H 50
Nakazawa S 3
Naruki Y 50
Nourse V 53
O'Reilly RJ 29
Ogasawara M 28
Ohtsuka S 50
Paglieroni T 9
Palacios R 33
Palutke M 4
Papamichael M 36
Payne SV 55
Peng R 9
Pernis B 12
Phaneuf JD 23
Pialat J 8
Pillemer E 22
Plummer JM 15
Rager-Zisman B 43
Reekers P 25
Reinherz EL 27
Reyes F 14
Robertson MD 46
Robinson DS 13
Roelcke D 10
Roos D 16
Rosen OM 43
Roth P 12
Saffold PC 54
Sale GE 41
Saunders PH 26
Schellekens PT 16
Schlossman SF 38
Schmidt TJ 45
Schneck J 43
Scholssman SF 27
Schott B 8
Shinbo T 50
Silver BA 49
Spiegelberg HL 15
Springer T 32
Stafford HA 17
Staughton RC 6
Stendahl O 35
Stevenson GT 13
Strominger J 19
Strong DM 7
Stutman O 56
Suzuki M 50
Swart K 42
Tabaczka P 4
Takane K 3
Takaoki M 52
Tanke HJ 16
Tarmin L 58
Tax WJ 25
Taylor SG 54
Ten Berge I 16
Terry WD 47
Thompson EB 45
Todd RF 38
Touraine F 8
Trillet M 8

Uno J. 21
Van de Griend R. 16
Vanhaelen CP. 49
Vogt A. 44
Ware CF. 26
Waters H. 11
Weissman I. 22
Wilkes BM. 5
Willems HW. 25
Williams D. 2
Wright DH. 55
Yamada K. 3
Yamamoto JK. 51
Yamamoto N. 44
Yeh CJ. 36




# More Than Just A Fancy Name

**Mention CANCERLINE to your librarian** and the world's foremost collection of cancer information is at your disposal. With the help of this computerized data system, you can obtain information on the following:

## Cancer Literature

The literature date base, **CANCERLIT**, allows you to survey more than 3,000 biomedical journals for information on your topic of interest. Your search will also alert you to meeting proceedings, monographs, and books published in that area. Informative abstracts averaging 200 words are provided with each citation;

## Current Cancer Research

The data base **CANCERPROJ** allows you to retrieve descriptions of current work in any cancer research area. The descriptions, which state research objective, methodology, and experimental results, are supplied for projects underway in 77 countries around the world.

## Cancer Therapy Protocols

The **CLINPROT** section of CANCERLINE is designed primarily for clinicians. It provides detailed summaries of currently active experimental protocols for any cancer site, agent, or type.

**Ask your biomedical librarian about CANCERLINE.**
CANCERLINE is sponsored by the international Cancer Research Data Bank—a program of the National Cancer Institute.

# VIDEOTAPES

## ON CURRENT TOPICS IN CANCER RESEARCH

A pilot project of the International Cancer Research Data Bank (ICRDB) Program of the National Cancer Institute

*Three series are available . . .*

### THE RELATION OF CARCINOGEN ACTION ON DNA TO CELL TRANSFORMATION

| | | |
|---|---|---|
| PETER MAGEE<br>Fels Research Institute | *Keynote Address* | #VK01<br>28 min. |
| JAMES K. SELKIRK<br>Oak Ridge National Laboratories | *Metabolic Activation and Macromolecular Binding of Chemical Carcinogens* | #VK02<br>51 min. |
| PHILIP C. HANAWALT<br>Stanford University | *Cellular Responses to Damaged DNA* | #VK03<br>54 min. |
| CHARLES HEIDELBERGER<br>University of Southern California | *Mutagenesis and Oncogenic Transformation of Mouse Embryo Cells* | #VK04<br>54 min. |
| FRED RAPP<br>Milton S. Hershey Medical Center | *The Interaction of Herpesviruses and Host Cells Leading to Latency or Transformation* | #VK05<br>52 min. |
| | *Panel Discussion* | #VK06<br>31 min. |

### MECHANISMS OF METASTASIS

| | | |
|---|---|---|
| ISAIAH FIDLER<br>Frederick Cancer Research Center | *The Heterogeneous Nature of Cancer Metastasis and Implications for Therapy* | #VB01<br>47 min. |
| GEORGE POSTE<br>Smith, Kline and French Laboratories | *Phenotypic Analysis of Metastatic Cell Populations* | #VB02<br>42 min. |
| LANCE LIOTTA<br>National Cancer Institute | *Tumor Cell Invasion of Basement Membranes and Extracellular Matrices* | #VB03<br>33 min. |
| EVERETT SUGARBAKER<br>Miami Cancer Institute | *Some Clinical Characteristics of Metastasis in Man* | #VB04<br>41 min. |

### AUTOMATED CYTOLOGY

| | |
|---|---|
| Part One: Principles and Techniques | #VB05<br>56 min. |
| Part Two: Biological Applications | #VB06<br>52 min. |

VIDEOTAPES ON CURRENT TOPICS IN CANCER RESEARCH are in the 3/4" U-matic format and can be played on video equipment which accepts the NTSC standard (the standard for videotapes produced in the U.S.). The two Automated Cytology tapes (#VB05 and #VB06) are also available in the PAL format.

The videotapes are available on a loan basis. If you would like to schedule viewing for your group, or for more information, please write to:

Videotape Coordinator
ICRDB Program
Westwood Building, Room 10A18
Bethesda, MD 20205

Please specify three choices for viewing dates, and the tapes desired.

**U.S. DEPARTMENT OF COMMERCE**
**National Technical Information Service**
5285 Port Royal Road
Springfield, Va. 22161

OFFICIAL BUSINESS

Penalty for Private Use, $300

**PRINTED MATTER**

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF COMMERCE
COM-211

THIRD CLASS
BULK RATE

U.S.MAIL

CB-17

**CANCERGRAMS** are distributed for the International Cancer Research Data Bank (ICRDB) by the National Technical Information Service (NTIS). **CANCERGRAMS** are available from NTIS on a standing order basis at $2 each for North American Continent addressees and $3 each for other addressees. An NTIS deposit account is required. For a list of subject categories or other information, please write to:

Subscription Section
National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161

**NOTICE OF MAILING CHANGE**

☐ Check here if you wish to discontinue receiving this publication

☐ Check here if your address has changed and you wish to continue receiving this publication. (Be sure to furnish your complete address including zip code.)

Tear off cover with address label still affixed and send to:

Computer Support Center
ICRDB Program
IIT Research Institute
10 West 35th Street
Chicago IL. 60616

CB 17/82/10

NCI/ICRDB/CB17 82/10

PB87-931810

# ICRDB CANCERGRAM

# IMMUNOBIOLOGY AND CANCER

## Identification and Characterization of Immune Cells

SERIES CB17 No. 82/10 OCTOBER, 1982

This Cancergram is a service of the INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM of the U.S. National Cancer Institute. Every few weeks, an updated Cancergram containing abstracts of selected cancer-related articles recently published in more than 3000 journals, and dealing with the topic indicated by the above title, is sent to researchers working in this area. These researchers are identified on the basis of the description of their current research project that has been submitted to the ICRDB Program, directly or via granting agencies.

This Cancergram is prepared by the Cancer Information Dissemination and Analysis Center (CIDAC) for Virology, Immunology, and Biology. ***If this Cancergram is useful and valuable, please send your comments to the CIDAC address below, since future editions depend on user satisfaction and user needs:***

CIDAC FOR VIROLOGY, IMMUNOLOGY, AND BIOLOGY
SCIENCE INFORMATION SERVICES
FRANKLIN INSTITUTE RESEARCH LABORATORIES
20TH AND RACE STREETS
PHILADELPHIA, PA 19103

NEWARK PUBLIC LIBRARY

NOV 19 1982

U. S. GOVT. PUBS.
DEPOSITORY 376

*In this issue:*


- **CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS..... 1-14**
- **DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS..... 15-22**
- **LYMPHOCYTE AND DIFFERENTIATION ANTIGENS..... 23-29**
- **CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION..... 30-36**
- **EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS..... 37-48**
- **OTHER RELATED STUDIES..... 49-60**


## CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS

### 1. LYMPHOCYTIC LEUKEMIA.

**Takiguchi T, Konda S**
**Dept. Hemato-Immuno-Internal Medicine, Kanagawa Medical Univ., Yokohama 52, Japan**
**Nippon Rinsho; 39(8):2741-2748 1981**

Since chronic lymphocytic leukemia (CLL) is the malignant proliferation of homogeneous mature lymphocytes, the morphological classification method of Rai based on clinical staging is widely used. For the classification of acute lymphocytic leukemia, (ALL) the FAB system has recently been drawing attention. This is based on the morphological observation of cells in Romanowsky stained specimen. In some cases, however, no numerical criteria are given, and therefore, a diagnostic consistency is difficult to obtain. Morphologically monotonous ALL, CLL, and other unclassifiable leukemia can now be further divided immunologically by detecting specific antigens, such as surface membrane Ig for B cells and pan-T for T cells. By checking the presence and types of complement receptors,



HE 20.3173/2:

further classification is possible. Monoclonal antibodies are useful for the analysis of T1, T2, ALL antigens and Ia antigen. The FAB classification cytochemically identifies myelocytic, monocytic, and ALL, and then classifies them by morphological appearance. In this sense, enzymological methods are important for the identification and classification of lymphocytic, myelocytic and monocytic leukemic cells. At this time, the classification methods are not yet complete. (30 Refs) (In JPN)

## 2. PROLYMPHOCYTIC LEUKEMIA OF HELPER CELL PHENOTYPE: REPORT OF A CASE AND REVIEW OF THE SCIENTIFIC LITERATURE.

Chan WC, Check IJ, Heffner LT, Gordon D, Whitsett C, Brynes RK
Dept. Pathology and Lab. Medicine, Emory Univ., Atlanta, GA, 30322
Am J Clin Pathol; 77(5):643-647 1982

A case of prolymphocytic leukemia was studied by using light and electron microscopy, cytochemistry and multiple immunological markers for T and B lymphocytes. Cytochemical and immunological studies showed that the cells were T-lymphocytes. By using monoclonal antibodies to human T-cell subsets, we found that these cells had the T-helper cell phenotype. The usefulness of multiparameter studies in subclassifying T-cell malignancies is discussed and the literature on T-prolymphocytic leukemia reviewed. (Author abstract) (37 Refs)

## 3. HUMORAL AND CELLULAR ASPECTS OF IMMUNOSUPPRESSION IN CHRONIC LYMPHOCYTIC LEUKEMIA (CLL): EFFECT OF REMISSION (MEETING ABSTRACT)

Sinclair TF, Ezdinli EZ, Hindo J
Chicago Medical School, North Chicago, IL, 60064
Proc Am Assoc Cancer Res; 23:1029 1982

Both cellular and humoral immune abnormalities are known to occur in CLL, but it is not yet known if they are related. Plasma from 20 untreated CLL patients was tested with lymphocytes isolated from the peripheral blood (PB) of normal controls for its effect on rosette formation with sheep red blood cells (E) and mitogenesis in the presence of phytohemagglutinin (PHA). Mean percent plasma inhibition values were not significant in the E-rosette assay but were in the PHA induced mitogenesis assay when compared to normal plasma. PB mononuclear cells from seven patients who possessed plasma inhibitors in the mitogenesis assay were analyzed for the relative proportions of T-lymphocyte subsets defined by indirect immunofluorescence using monoclonal antibodies OKT-3, OKT-4, and OKT-8. All of these patients had both an increase in the suppressor cell subset OKT-8 and a decrease in the helper cell subset OKT-4, the relative proportions in PB being 12.0% and 5.8% respectively. The B cell character of these patients lymphocytes was demonstrated by a relative lack of reactivity to OKT-3 and by direct immunofluorescence for surface immunoglobulin. Two patients in this series have achieved complete remission and preliminary data indicates that the proportion of the helper and suppressor cell subsets in the PB return to normal, but that their plasmas retain inhibitory activity in the mitogenesis assay. (no Refs)

## 4. PROGNOSIS OF CHRONIC LYMPHATIC LEUKEMIA.

Leporrier M
Service hematologie-cliniques, C.H. regional et universitaire, boulevard G. Clemenceau, 14040 Caen Cedex, France
Gaz Med Fr; 89(12):1323,1326,1329 1982

Median survival for patients with chronic lymphocytic leukemia (CLL) is discussed in relation to the number of lymphoid sites involved, the presence and degree of anemia and/or thrombopenia, and other factors such as age, sex, lymphocytosis, type of bone marrow infiltration, involvement of retroperitoneal lymph nodes, in vitro response to phytohemagglutinins, PAS markers, and levels of serum immunoglobulins. A classification scheme is presented to predict survival of CLL patients, based on lymphoid involvement and presence of anemia and/or thrombopenia. Treatment of CLL patients is discussed, based on prognosis. (7 Refs) (In FRE)

## 5. THE ASSOCIATION OF HAIRY CELL LEUKEMIA WITH UNUSUAL IMMUNOLOGIC DISORDERS.

Dorsey JK, Penick GD
Dept. Internal Medicine, Univ. Iowa Hosp. and Clinics, Iowa City, IA, 52242
Arch Intern Med; 142(5):902-903 1982

Hairy cell leukemia is a rare disease, probaoly of B-lymphocyte origin, that has been reported to rarely occur with polyarteritis nodosa. The records of 31 patients with hairy cell leukemia were reviewed for an association with other disorders of the immune system; such an association was found more often than previously suspected. Four cases are discussed - one with hepatitis B surface antigen-positive polyarteritis nodosa and another with an IgA (kappa) monoclonal gammopathy and amyloidosis of the kidney, liver, and small bowel. The other two patients had cutaneous vasculitis, one of which was a rare form of leukocytoclastic angiitis - erythema elevatum diutinum. Because the number of patients in this study is small, it is impossible to say whether the association of hairy cell leukemia with any of these immunologic disorders adversely affects survival. (Author abstract) (13 Refs)

## 6. IDEOTYPIC STUDY IN HUMAN MYELOMA.

Boccadoro M, Gavarotti P, Massaia M, Pileri A
Istituto di Medicina Interna, Universita di Torino, Via Genova, 3, 10126 Turin, Italy
Minerva Med; 73(18):1175-1178 1982

Immunological studies on human myeloma and benign monoclonal gammopathy are reviewed. Increased number of monoclonal B cells, which are the stem cells, are present even during complete remission from myeloma. Distinct tumors markers are present in myeloma and benign monoclonal gammopathy, which permit the cells involved to be identified. (27 Refs) (In ITA)

## 7. IDIOTYPE-BEARING LYMPHOID CELLS IN PLASMA CELL NEOPLASIA.

Mellstedt H, Holm G, Pettersson D, Peest D
Dept. Radiobiology, Karolinska Hosp., S-10401 Stockholm, Sweden
Clin Haematol; 11(1):65-86 1982

Current evidence for the existence of B lymphocytes as part of the tumor cell clone in multiple myeloma (MM) is discussed and related to tumor cell differentiation and progression. B lymphocytes carrying the light chain isotype of the myeloma protein are selectively increased in the blood of approx half of untreated patients and are also found in the bone marrow when not detected in peripheral blood. Further evidence for the existence in MM of monoclonal B lymphocytes is provided by the varying expression of IgG-Fc- and C3-receptors on idiotypic cells; the presence of idiotypic Ig in some cell cytoplasm; and the morphology of lymphocytes, lymphoplasmacytoid cells, or plasma cells. (60 Refs)

## 8. CHARACTERISTICS OF HODGKIN'S DISEASE-DERIVED CELL LINES.

Diehl V, Kirchner HH, Burrichter H, Stein H, Fonatsch C, Gerdes J, Schaadt M, Heit W, Uchanska-Ziegler B, Ziegler A, Heintz F, Sueno K

Hamatologie/Onkologie, Medizinische Hochschule, Karl-Wiechert-Allee 6, 3000 Hannover, W. Germany

Cancer Treat Rep; 66(4):615-632 1982

In the last 3 yr we were able to establish five long-term in vitro cell cultures from biopsy specimens taken preterminally from four patients with histologically proven Hodgkin's disease (nodular sclerosing type, clinical Stage IVB). Four of the lines are continuously proliferating in vitro; one culture stopped growth for unknown reasons after 7 months. When culture conditions were modulated, the first culture, L 428, gave rise to two sublines: L 428 KS, after adaptation to calf serum, and L 428 KSA, permanently growing as an adherent monolayer line after treatment with a phorbol ester (12-O-tetradecanoylphorbol-13-acetate) for 3 wk. Cell-marker analysis by conventional means (SIg, cIg, rosette formation, Epstein-Barr virus reactivity, cytochemistry, phagocytosis, and lysozyme production) and with monoclonal antibodies directed against various human lymphoid, myeloid, and monocytoid antigens showed that the tested cell lines are clearly different from all hitherto described hematopoietic lines; they most likely represent a cell type resembling an early myeloid-monocytoid progenitor cell. Conditioned medium of the L 428 cells and its two sublines showed colony-stimulating factor activity and suppression of spontaneous cell-mediated cytolysis of L 428 KS and K 562 cells. (Author abstract) (26 Refs)

## 9. IMMUNOHISTOCHEMICAL CLASSIFICATION OF NON-HODGKIN'S LYMPHOMAS USING MONOCLONAL ANTIBODIES (MEETING ABSTRACT)

Borowitz MJ, Crocker BP

Department of Pathology, Duke University Medical Center, Durham, NC, 27710

Am J Clin Pathol; 77(2):247 1982

Immunologic classification of non-Hodgkin's lymphomas (NHL) usually has relied on analyzing suspensions of cells teased from tumors. This procedure requires special technics and may not yield a representative sample in some cases. Lymphocyte markers may also be detected on frozen tissue sections. We stained nine cases of HNHL by an indirect immunoperoxidase (IP) technique for SIg, and with monoclonal antibodies against Ia(HLADR), pan-T(0KT3,Leu1),T-Help(Leu3a),T-Sup(Leu2a,0KT8), and thymic (0KT6) antigens. Tumor cell suspensions also were studied in immunofluorescence and cytotoxicity. In four cases the suspensions contained mixed B and T cells; in section these had areas of tumor with partially preserved node. In three of these the tumors cells stained for SIg and/or Ia(B cell), while the fourth stained only with OKT3 and Leu3a. The remaining five cases were homogeneous and the section and suspension data agreed. These included two large cell lymphomas, one with both pan-T and Ia antigens; one CLL and one lymphoblastic lymphoma with identical T and thymic antigen phenotypes, and one B-lymphoblastic lymphoma. IP detection of lymphocyte surface antigens makes immunologic classification of HNHL more readily available in the pathology laboratory and is particularly useful in studying complex tumors with subtotal node involvement. (no Refs)

## 10. LYMPHOSARCOMA WITH LEUKEMIA IN A HORSE.

Madewell BR, Carlson GP, MacLachlan NJ, Feldman BF

Dept. Veterinary Pathology, Veterinary Sch., Univ. Glasgow, Bearsden, Glasgow G61 1QH, Scotland

Am J Vet Res; 43(5):807-812 1982

A 17-yr-old Arabian gelding was presented because of CNS depression and wt loss. Physical examination revealed generalized lymphadenopathy, pitting edema, and ascites. The diagnosis of lymphosarcoma with leukemic manifestations was based on cytologic and histopathologic examination of lymph node biopsy samples and a peripheral leukocyte count of 98,300/ul, 94% of which were mature lymphocytes. These circulating lymphocytes lacked B-lymphocyte markers and did not respond to mitogenic stimulation, indicating functional incompetence. Though ultrastructural findings were equivocal, most morphologic changes indicated these cells were of T-lymphocyte lineage. Virus particles were not observed during transmission electron microscopy of these lymphocytes. (Author abstract) (29 Refs)

## 11. SELECTIVE T LYMPHOCYTE SUBSET PROLIFERATION IN 'LYMPHOMATOID GRANULOMATOSIS' (MEETING ABSTRACT)

Petras R, Tubbs R, Sebek B, Gollsh J, Savage R, Weiss R, Welck J

Cleveland Clinic Foundation, Cleveland, OH

Lab Invest; 46(1):65A 1982

Four cases of lymphomatoid granulomatosis (LYG) were studied by histochemistry, electron microscopy, frozen and paraffin section immunohistochemistry for immunoglobulin light chains and muramidase, and frozen section immunohistochemistry using monoclonal antibodies to evaluate the expression of lymphocyte differentiation antigens by the proliferating cells. The pulmonary lesions demonstrated polyclonal kappa and lambda immunostaining. However, only a few cells were positive for surface or cytoplasmic immunoglobulin. Cytologic atypical large lymphoid cells invariably contained cytoplasmic immunoglobulin of one light chain type and did not express T lymphocyte differentiation antigens. Most of the infiltrate was composed of cytotoxic/suppressor T lymphocytes (as demonstrated using monoclonal hybridoma antibodies) and esterase-and muramidase-positive tissue macrophages. No extracellular immune complexes were demonstrated. Based on these observations, we postulate that the early lesions of LYG most likely represent either a T cell lymphoproliferative or possibly an autoimmune disorder having manifestations of cellular immunity or antibody-dependent cellular cytotoxicity. Reports of B cell immunoblastic sarcoma complicating LYG probably represent persistent immunologic stimulation with emergence of neoplastic B cell clones. (no Refs)

## 12. SURFACE GLYCOPROTEINS OF MALIGNANT HUMAN LEUKOCYTES.

Gahmberg CG, Andersson LC

Dept. Biochemistry, Univ. Helsinki, Helsinki, Finland

Biochim Biophys Acta; 651(2/3):65-83 1982

The biochemistry of cell surface glycoproteins of malignant WBC is reviewed. Topics discussed include surface glycoproteins of normal hematopoietic cells, cultured cell lines for malignant WBC (Epstein-Barr virus positive and negative lymphoma cell lines, histiocytic lymphoma lines, T cell leukemia, non-T, non-B cell leukemia, hairy cell leukemia, erythroleukemic cell line K562, the HL-60 promyelocytic cell line), and

surface glycoproteins from patients with leukemias and lymphomas. (138 Refs)

### 13. PHENOTYPING HUMAN LEUKEMIC T-CELL LINES: ENZYME MARKERS, SURFACE ANTIGENS AND CYTOGENETICS.

Martin PJ, Giblett ER, Hansen JA
Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104

Immunogenetics; 15(4):385-398 1982

We have compared phenotypic markers for a series of established human leukemic T-cell lines collected from different laboratories. Cell lines were tested first for genetic markers using polymorphic enzymes and then for expression of T lymphoid cell surface differentiation antigens using monoclonal antibodies. Chromosomal analysis was used as an additional method for identification of selected cell lines. On the basis of enzyme markers, it was possible to assign each of the cell lines examined to one of nine different groups. With two exceptions, surface antigen phenotypes for each of 12 cell lines were clearly distinctive. Thus, some groups of cell lines indistinguishable by enzyme markers could be further subdivided by surface antigen phenotyping. However, significant quantitative variation in expression of individual antigens was observed. In addition, surface antigen expression was not uniform in different subcultures of one cell line studied in detail. These results indicate that leukemic T-cell lines cannot be used generally as simple models of surface antigen expression in normal T-cell differentiation. (Author abstract) (38 Refs)

### 14. PHORESIS OF TUMOR CELLS.

Shishido H
Third Dept. Internal Medicine, Dokkyo Medical Univ., Saitama Prefecture, Japan

Nippon Rinsho; 39(8):2856-2861 1981

By measuring migration speed and cell surface changes in cell electrophoresis, properties of membrane surface and membrane phenomena can be studied. From a histogram of the migration speed of peripheral blood cells obtained from 50 healthy adults, 3 peaks,-0.75+-0.09 (S),-0.89+-0.17 (F), and-1.17+-0.06 (R) micro/sec/v/cm were obtained. In various non-cancerous hematopoietic diseases, when leukocytes were electrophoresed, F peak increased in lymphocytosis, whereas S peak increased in neutrophilia. In contrast, in acute leukemia, abnormal peaks, different from S and F peaks, are noted. A similar abnormal peak was obtained in acute myelocytic leukemia, acute lymphocytic leukemia, acute monocytic leukemia, and acute premyelocytic leukemia, despite their morphological differences. In chronic myelocytic leukemia, a tendency to disperse toward high speed from normal S peak was clearly seen; and an abnormal peak similar to that of other acute leukemia was also seen. Normal lymphocytes showed an F peak with faster T cell migration speed than B-cell. Lymphocytes from various leukemias clearly exhibited abnormal peaks, suggesting that electrophoretic properties may serve as a tool for studying malignancy. These abnormal peaks rapidly decreased as therapy progressed. Therefore, electrophoretic mobility can also be used to judge therapeutic effects. (28 Refs) (In JPN)

## DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS

### 15. HUMAN NEUTROPHIL FCGAMMA RECEPTOR DISTRIBUTION AND STRUCTURE.

Fleit HB, Wright SD, Unkeless JC
Dept. Cellular Physiology and Immunology, Rockefeller Univ., New York, NY, 10021

Proc Natl Acad Sci USA; 79(10,part1):3275-3279 1982

Fc receptors (FcR) for IgG on human cells were analyzed with two monoclonal antibodies, 3G8 and 4F7. Fab fragments of both hybridoma IgGs inhibited binding to neutrophils of soluble rabbit IgG complexes and sheep erythrocytes (E) coated with rabbit IgG. The number of sites for 3G8 Fab was 135,000 per neutrophil, roughly equivalent to the number of sites for rabbit IgG in immune complexes (112,000 per cell). We did not observe human IgG1 binding sites on neutrophils, although binding of IgG1 to FcR-bearing lines U937 and HL-60 was readily demonstrated. Other cell types bearing 3G8 binding sites were mature chronic myelogenous leukemia cells, eosinophils, 6% of E-rosetting lymphocytes, and 15% of Ig-bearing peripheral lymphocytes. No binding of 3G8 Fab was observed on the FcR-bearing cell lines U937, HL-60, Raji, Daudi, and K562 or on blood monocytes. However, 15% of monocytes cultured for 7 days and 60% of lung macrophages expressed 3G8 antigen. When analyzed by sodium dodecyl sulfate/polyacrylamide gel electrophoresis, the neutrophil FcR immunoprecipitated with 3G8 or 4F7 Fab-Sepharose displayed a broad band extending from Mr 73,000 to 51,000; in many experiments this band was resolved into two poorly separated components, centered at Mr 66,000 and 53,000. These results show that human neutrophil FcR for IgG is different from that on monocytes, with respect to both antigenic composition and binding of monomeric IgG1. (Author abstract) (35 Refs)

### 16. STUDY OF IGE AND IGG FC SURFACE RECEPTORS ON MOUSE MASTOCYTOMA CELLS (MEETING ABSTRACT)

Basciano LK, Siraganian RP, Isersky C
National Institutes of Health, Bethesda, MD, 20205

Fed Proc; 41(3):825 1982

The mastocytoma cell line MMC-1 derived from a tumor in CXBI mice releases histamine with both IgE and IgG mediated reactions. The nature of the Fc(epsilon) and Fc(gamma) receptors on these cells was investigated. To study the Fc(gamma) receptor we used a rabbit antiserum of the IgG2b receptor on the mouse macrophage P388D cell line. The Fc(epsilon) receptors were assayed using either rat IgE or rabbit antiserum to the Fc(epsilon) receptor of rat basophil leukemia cells. Fluorescent studies demonstrated simultaneous binding of rat IgE and antiserum to Fc(gamma) receptors, thus a single cell expressed both Fc(epsilon) and Fc(gamma) cell surface receptors. Cells were surface labeled with 125I, the membranes solubilized, and the Fc-IgG and Fc-IgE receptors immunoprecipitated and analyzed on sodium dodecyl sulfate polyacrylamide gels. IgE and anti-IgE or rabbit anti-Fc (epsilon) precipitated a broad band of protein with an apparent molecular weight of approx 60K. Anti-Fc-IgG antiserum precipitated a similar protein peak with a slightly higher apparent molecular weight (68-74K). By sequential immunoprecipitation, removal of the membrane component(s) reacting with rat IgE or antiserum to the Fc(epsilon) receptor left behind a component(s) precipitating with anti-Fc(gamma). Therefore, the FC(epsilon) and Fc(gamma) receptors are antigenically dis-

tinquishable and appear to be separate cell membrane components. (no Refs)

## 17. PHENOMENON OF HUMAN T CELLS ROSETTING WITH SHEEP ERYTHROCYTES ANALYZED WITH MONOCLONAL ANTIBODIES: MODULATION OF A PARTIALLY HIDDEN EPITOPE DETERMINING THE CONDITIONS OF INTERACTION BETWEEN T CELLS AND ERYTHROCYTES.

**Bernard A, Gelin C, Raynal B, Pham D, Gosse C, Boumsell L**
**Laboratoire d'Immunologie des Tumeurs de l'Enfant, Institut Gustave-Roussy, 94800 Villejuif, France**
**J Exp Med; 155(5):1317-1333 1982**

The monoclonal antibody (MAb) anti-D66, which identifies an epitope that appears to be involved in E-rosette formation, is described. Unlike MAb 9.6, anti-D66 does not block rosettes when erythrocytes have been pretreated with neuraminidase or 2-aminoethylisothiouronium bromide, although it blocks E-rosettes made at both 4 C and 37 C. Cell surface molecules from thymocytes were labeled and isolated by immunoprecipitation and acrylamide gel electrophoresis. D66 and 9.6 epitopes were carried by the same molecule, and although 9.6 epitopes were readily exposed on the cell surface, a large fraction of the D66 epitopes was covered by the glycocalix, from which it can be unmasked by anti-D66 sensitization plus anti-mouse immunoglobins. D66 is an epitope involved in the interactions between T lymphocytes and erythrocytes, and is clearly different from the epitope defined by MAb 9.6. A striking correlation was observed between the surface density of D66 in a given T cell population and its ability to form stable rosettes at 37 C. (48 Refs)

## 18. COMPLEMENT (C3) RECEPTORS ON DENDRITIC RETICULUM CELLS OF NORMAL AND MALIGNANT LYMPHOID TISSUE.

**Gerdes J, Stein H**
**(c/o Stein) Inst. Pathology, Christian Albrecht Univ., Hospitalstr. 42, D-2300 Kiel, W. Germany**
**Clin Exp Immunol; 48(2):348-352 1982**

The aim of this study was to investigate whether dendritic reticulum cells (DRC) in normal lymphoid tissue and in malignant non-Hodgkin's lymphomas possess receptors for the third complement component (C3 receptors). For this purpose we studied the in situ expression of C3 receptors in lymphoid tissue by staining frozen tissue sections with an antiserum specific for human C3 receptors (AC3RS), using a modified immunoperoxidase method. The results indicate that DRC of normal and malignant lymphoid tissue express large amounts of C3 receptors. Absorption experiments revealed that the C3 receptors of DRC are identical with, or at least share common antigenic sites with, the C3 receptors expressed by tonsil B cells. (Author abstract) (17 Refs)

## 19. ANTI-IDIOTYPES TO MONOCLONAL ANTI-H-2 ANTIBODIES - I. CONTRIBUTION OF ISOLATED HEAVY AND LIGHT CHAINS TO IDIOTYPE EXPRESSION.

**Bluestone JA, Metzger JJ, Knode MC, Ozato K, Sachs DH**
**Translation Biology Section, Immunology Branch, NCI, NIH, Bethesda, MD, 20205**
**Mol Immunol; 19(4):515-524 1982**

Anti-idiotypic sera were produced by immunization of miniature swine with affinity-purified monoclonal anti-H-2Kk antibodies. The purified anti-idiotypic antibodies obtained by this immunization recognized unique determinants on each monoclonal anti-H-2Kk immunogen and were not broadly cross-reactive with other anti-H-2Kk antibodies. These reagents were used to examine the expression of idiotype on isolated heavy and light chains as well as on reassociated Ig molecules. Minor populations of idiotope(s) could be detected by a direct binding radioimmune assay on isolated heavy chains and on isolated light chains. However, the predominant idiotope(s) were expressed only on native Ig and on isolated heavy chains. The expression of these heavy-chain idiotopes was found to be specifically augmented by the addition of homologous light chains. In contrast, reassociation of heavy chains with light chains from a different anti-H-2Kk monoclonal antibody diminished idiotype expression. A model for the molecular interactions occurring between these molecules is proposed on the basis of these results. The nature of these interactions may also have implications for the analysis of the basis of idiotype expression on anti-MHC T-cell receptors. (Author abstract) (26 Refs)

## 20. DIFFERENCES IN THE HORMONAL STIMULATION OF NORMAL AND LEUKEMIC HUMAN PERIPHERAL LEUKOCYTES (MEETING ABSTRACT)

**Paletta E, Schwarzmeier JD**
**First Medical Department, University of Vienna, Vienna, Austria**
**12th Workshop on Leukocyte Cultures, February 14-17, 1982, Vienna, Austria Wiener Medizinische Akademie; :A69 1982**

We have measured the density of beta-adrenoceptors and the stimulation of adenylate cyclase (AC) by the beta-adrenergic agonist isoproterenol (INE), prostaglandin E1 (PGE1) and histamine (HIS) in normal as well as leukemic leukocytes. The number of beta-adrenoceptors on intact cells was determined using the beta-adrenergic antagonist 125I-iodohydroxybenzylpindolol (IHYP) as radioligand. One single class of high affinity binding sites for IHYP was identified on normal lymphocytes, monocytes and polymorphonuclear leukocytes (PMN). Maximal binding of IHYP, ie the quantity of beta-adrenoceptors present did not differ significantly among normal leukocytes. Fractionation of lymphocytes into B- and T-cells revealed significantly higher beta-receptor numbers on B than on T cells. Among leukemic cells tested, blast cells from AMOL (acute monocytic leukemia) and AMMOL (acute myelomonocytic leukemia) patients usually exhibited much higher beta-receptor densities than those from AML (acute myelocytic leukemia), and beta-receptor numbers were lowest in CLL (chronic lymphocytic leukemia) and ALL (acute lymphocytic leukemia). AC activity measured as cyclic adenosine 3', 5' - monophosphate (cAMP) produced per mg protein per min was studied in cell membrane preparations. Despite the fact that beta-receptors numbers were comparable in lymphocytes, monocytes and PMN, the latter showed a much weaker response to INE, but also to PGE1 and HIS. Results obtained using GTP and NaF as positive effectors of AC indicate that the poor hormonal responsiveness of PMN might be due to an impaired coupling between hormone receptors and catalytic unit of AC. Normal B lymphocytes showed a marked increase in cAMP production upon stimulation with INE, whereas T cells failed to respond. This relates to the different numbers of receptors identified on the two cell types. Among leukemic cells, the effectiveness of INE to stimulate AC corresponded to the beta-receptor numbers found to be present. AC reactivity to PGE1 and HIS followed the pattern of response to INE. (no Refs)

## 21. NATURALLY OCCURRING CYTOTOXIC CELLS (MEETING ABSTRACT)

**Riethmuller G**

**Institut fur Immunologie der Universitat Munchen, Munchen, W. Germany**

**9th International RES Congress, February 7-12, 1982, Davos, Switzerland. American Reticuloendothelial Society 68 pp., 1982.**

From its beginning, the field of natural cytotoxicity has been beset by two major problems which have a direct bearing on the continuing quest for the in vivo relevance of this spontaneous cytocidal mechanisms. Firstly, the remarkable phenotypic heterogeneity of NK (natural killer) cells has remained until recently one of the intriguing open questions. The other problem concerns the as yet unknown recognition mechanisms and the undefined membrane structures on the target cells. Many efforts have been undertaken to define the relationship of NK cells to the three main classes of lymphoid cells, ie macrophages, T-cells and B-cells. This problem has become amenable quite recently with the help of monoclonal antibodies and by cloning of effector cells. The designation of NK cells as null cells has been revised for several species. Thus, in the mouse promonocytes have been characterized as NK cells with a defined spectrum of susceptible target cells. However, other findings point to a considerable heterogeneity which shows that NK cells express Thy1 antigens as well as Ly related antigens characteristic for the T cell lineage. The expression of Fc receptor remains controversal since Fc receptors may be absent on some NK cells depending on their organ origin. In man, large granular lymphocytes (LGL), as a characteristic minor subpopulation, seem to account for the whole NK activity. Analysis with monoclonal antibodies revealed that malignant cells as well as normal cells with the LGL appearance may express a hybrid phenotype ie they show simultaneous expression of thymus-associated and monomyelocytic-associated antigens. This finding on human cells may shed light on the unusual heterogeneity observed in mice where NK cells with monocytic and thymic phenotypes have been discerned. (no Refs)

## 22. THE ROLE OF NK CELLS IN RESISTANCE OF IN VIVO TUMORS (MEETING ABSTRACT)

**Okumura K, Habu S, Kasai M**

**1 Department of Immunology, University of Tokyo, Tokyo, Japan**

**9th International RES Congress, February 7-12, 1982, Davos, Switzerland. American Reticuloendothelial Society 68 pp., 1982.**

The significance of natural killing of tumor cells by lymphocytes. previously investigated in limited in vitro phenomena has now been broadened by examining mechanisms of in vivo tumor resistance. Although the origin and differentiation pathway of murine natural killer (NK) cells is not clearly defined, NK cells express the glycolipid marker asialo GM1 which is not expressed on mature T or B cells. To study the role of NK cells in the incidence and growth of various tumors, we took advantage of the fact that microliter amounts of intravenously injected anti-asialo GM1 antibody could abolish NK activity in vivo. In nude mice, with reduced NK activity due to injection of anti-asialo GM1 antibody, the incidence of tumor take and growth of transplanted syngeneic (RL male 1), allogeneic (YAC-1) and human tumors was enhanced: An enhanced incidence of tumor take was also observed in the nude rat after depletion of NK activity by anti-asialo GM1 injection. Furthermore, growth of chemically induced autochtonous tumors was enhanced in nude mice after administration of anti-asialo GM1 antiserum. Based on the above observations, the biological role of NK cells in vivo will be discussed. (no Refs)

# LYMPHOCYTE AND DIFFERENTIATION ANTIGENS

## 23. NEW TYPE OF HUMAN LEUKEMIA-ASSOCIATED CELL MEMBRANE ANTIGEN AS IDENTIFIED BY MONOCLONAL ANTIBODIES (MEETING ABSTRACT)

**Seon BK, Negoro S**

**Department of Molecular Immunology, Roswell Park Memorial Institute, Buffalo, NY, 14263**

**Fed Proc; 41(3):2310 1982**

Milligram quantities of a human leukemia-associated cell membrane antigen (HL-CMA) preparation were isolated from the cell membranes of MOLT-4 (a T leukemia cell line) by means by a novel system of purification. A portion of the isolated HL-CMA preparation was utilized for obtaining mouse monoclonal hybridoma (MH) antibodies. An efficient radioimmunoassay was developed to identify hybridomas that generate MH antibodies directed toward HL-CMA. Appropriate hybridomas were cloned and 4 of the many resultant hybridoma clones, ie, G2/E12, G4/H3, H3/C9 and N6/D11, were tested by the radioimmunoassay against a variety of cells and cultured cell lines. These cell specimens include 6 T leukemia cell lines, 2 non-T/non-B leukemia cell lines, 2 pre-B leukemia cell lines, 1 myelocytic leukemia cell line, 3 B non-malignant cell lines, normal thymocytes (2 specimens from different donors) and normal PBL T cells (2 specimens). Culture fluids of all 4 hybridoma clones showed significant reactivity against only the T leukemia cell lines. Rabbit antisera prepared against the HL-CMA preparation showed the same specificity as those of the above MH antibodies. The antigen(s) detected by the present MH antibodies as well as by rabbit antisera appears to represent a new type of human T leukemia-associated cell surface antigen(s). (no Refs)

## 24. MONOCLONAL ANTIBODY BA-1 DOES NOT BIND TO HEMATOPOIETIC PRECURSOR CELLS.

**Jansen J, Ash RC, Zanjani ED, LeBien TW, Kersey JH**

**(c/o Kersey), Univ. Minesota, Box 609 Mayo, 420 Delaware St. S.E., Minneapolis, MN, 55455**

**Blood; 59(5):1029-1035 1982**

Monoclonal antibody BA-1 binds to B-lymphocytes, to cells from most cases of non-T acute lymphoblastic leukemia (ALL), and weakly to neutrophils. To determine whether BA-1 also reacts with hematopoietic progenitor cells (HPC), we studied the effect of removal of BA-1+ cells from human bone marrow on the proliferation in vitro of the trilineage precursor cell CFU-GEMM, and of the committed progenitor cells of granulopoiesis (CFU-C) and erythropoiesis (BFU-E/CFU-E). Complement-mediated cytotoxicity using BA-1 at concentrations far beyond those required to lyse BA-1+ bone marrow cells and ALL cells did not result in inhibition of colony formation in any of the assays. A rosette separation method, using ox red blood cells coated with BA-1, resulted in enrichment of HPC in the BA-1-depleted interface, whereas very few HPC were found in the BA-1-enriched pellet. Both methods indicate that BA-1 does not bind to HPC, although binding of the antibody to the lymphohematopoietic stem cell cannot be excluded yet. The high cytotoxic capacity of the IgM antibody BA-1, and the lack of reactivity with HPC, make the antibody particularly suitable for use in autologous bone marrow transplantation for patients with ALL. (Author abstract) (26 Refs)

## 25. REVERTANT EXPRESSING A STRUCTURAL VARIANT OF T200 GLYCOPROTEIN.

Hyman R, Trowbridge I, Stallings V, Trotter J
Dept. Cancer Biology, Salk Inst., Box 85800, San Diego, CA. 92138
Immunogenetics; 15(4):513-520 1982

The BW5147(T200-a) mutant, a T200-mutant derived from the T200 glycoprotein-positive T-cell lymphoma BW5147, was mutagenized with gamma-irradiation. Thirteen days later 1 x 10(7) cells were stained with 13/2.3 monoclonal T200-specific antibody and fluorescein-labeled goat anti-rat immunoglobulin and sorted for the most fluorescent 0.2% of cells. After fourth sorting, a detectable antigen-positive population was seen. The antigen-positive cells were split into two groups: line 1 and 2 were the most fluorescent 0.8% and 0.1%, respectively. The two lines were grown up and resorted separately and each line was cloned by limit dilution. Two clones, BW5147 x REV(T200-a) 1.1 and BW5147 x REV (T200-a)2.5, derived from lines 1 and 2, respectively, are described. The structure of the T200 glycoprotein found on the surface of the revertant cell lines was investigated by isolation of the molecule from lysates of radioiodinated cells by immunoprecipitation with monoclonal T200-specific antibody and analysis on polyacrylamide gels. The T200 glycoproteins (mol wt 105,000) isolated from the two revertant clones were much smaller than the wild-type molecule (mol wt 200,000). Results of 21P-labeling and tryptic cleavage and peptide mapping suggested that the major portion of the revertant T200 molecule is in the region of the wild-type molecule external to the plasma membrane. The implications of the such findings are discussed. (18 Refs)

## 26. EXPRESSION IN LARGE AMOUNTS OF BOTH I-A AND I-E ANTIGENS ON THE MURINE B-CELL LEUKEMIA, BCL1.

Letarte M, Meghji G, Lorimer G
Div. Immunology, Res. Inst., Hosp. Sick Children, 555 University Ave., Toronto M5G 1X8, Canada
Mol Immunol; 19(4):557-564 1982

The level of Ia antigens present on a murine B cell leukemia, passaged in BALb/c mice and designated BCL1, was measured in the cellular radioimmunoassay. Leukemic cells obtained from spleens of mice inoculated 4 wk previously with the tumor were shown to express, on a per cell basis, 14x more Ia than control BALB/c spleen cells. The wet wt of a leukemic spleen was approx 18x more than that of a control spleen. Several preparations yielded, on the av, 110x more Ia per leukemic mouse spleen than per control spleen. This augmentation suggests that BCL1 leukemic spleens are an abundant source for the purification of murine Ia antigens. Contrary to a previous report, I-Ad antigens could be demonstrated on BCL1 cells. Ib cells, which do not express I-E antigens on their surface shared with BCL1 cells Ia specificities recognized by A-TH anti-A-TL serum. Furthermore a monoclonal antibody to Ia-15-like specificity of I-A subregion was reactive with BCL1 cells. I-Ed antigens, as reported previously, were also present on BCL1 cells: 0.7 x 10(6) molecules of RAM-Fc were bound per BCL1 cell incubated with either of two independently derived monoclonal antibodies to Ia-7-like specificity. Immunoprecipitation of 125I-labeled Ia enriched fractions with either A-TH anti-A-TL serum or with monoclonal antibodies directed at I-Ad or I-Ed antigens yielded a major radioactive band of mol wt 28,000 under non-reducing conditions and of mol wt 34,000 under reducing conditions. (Author abstract) (26 Refs)

## 27. HUMAN PERIPHERAL BLOOD T CELLS EXPRESS DETERMINANTS RECOGNIZED BY A MONOCLONAL ANTIBODY DIRECTED AGAINST IA-LIKE (HLA-DR) MOLECULES (MEETING ABSTRACT)

Bertoglio J, Pinatel C
INSERM U. 218, Centre Leon Berard, Lyon, France
Hybridoma; 1(2):196 1982

Monoclonal antibodies were raised by somatic hybridization of murine myeloma cells (SP2/0) with spleen cells from Balb/c mice immunized with human T lymphocytes grown in IL2-containing conditioned medium. A number of hybridoma clones recognizing cell surface antigens on the immunizing cell were obtained. One of them (H4/104-2) produces an IgG2 antibody which, when used in a protein A binding assay, reacted with cultured B cell lines, IL2 dependent T cell lines and not with cultured leukemic T cell lines or the myeloid K562 cell line. It did not react with either human thymocytes, polymorphonuclear or platelets. This tissue distribution suggested that H4/104-2 antibody recognized Ia-like molecule. RIP-PAGE analysis of 125 Iodine labelled membrane extracts showed that H4/104-2 antibody precipitated a bimolecular complex of apparent molecular weight 28,000-34,000 daltons. However, when studied by other techniques this antibody was shown to strongly react not only with peripheral B cells, but also with up to 80% peripheral resting T lymphocytes. Subcloning, as well as absorption experiments clearly ruled out the possibility of the antibody not being monoclonal. When this antibody was cotitrated in a protein A binding assay versus another well defined anti-Ia monoclonal antibody (BL2), it was found that the two antibodies could bind simultaneously to B cell lines and to IL2 dependent T cell lines, yielding counts equal to the sum of each antibody tested separately, suggesting they recognize different determinants on the molecule. This antibody is not mitogenic for peripheral T lymphocytes and does not inhibit their PHA or CON A (phytohemagglutinin or conconavalin A) response nor the response of cultured T cells to IL2. In contrast it was found to strongly inhibit mixed lymphocyte cultures when added to the test at dilution up to 1:1000. (no Refs)

## 28. CHARACTERIZATION OF THE ANTIBODIES IN NORMAL RABBIT SERUM RESPONSIBLE FOR THE LYSIS OF NK-SENSITIVE TARGET CELLS.

Urdal DL, Henney CS
Basic Immunology Program, Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
Mol Immunol; 19(4):599-608 1982

Normal rabbit serum has previously been reported to lyse a spectrum of murine lymphoid cell lines characterized by being susceptible to natural killer (NK) cells. Although we have failed to confirm that a simple correlation exists between the susceptibility of target cells to NK cells and to normal rabbit serum, we were able to characterize a number of naturally occurring anti-carbohydrate antibodies which selectively lyse NK-susceptible lymphoma cells. The antibodies present in normal rabbit serum responsible for lysing an NK susceptible clone derived from the DBA/2 lymphoma L5178Y (27v-IC2) were found to be directed against the terminal beta-N-acetylgalactosamine sugar present on the neutral glycolipid gangliotriosylceramide. Interestingly, normal rabbit serum did not lyse an NK-insusceptible variant, derived from the same lymphoma, which lacked gangliotriosylceramide. YAC-1 target cells, the prototype target for murine NK cells, were insusceptible to normal rabbit serum. However, following neuraminidase treatment, such cells were lysed by an antibody in normal serum directed against terminal beta-galactose residues. The

anti-beta-galactose reactivity was directed against the carbohydrate structure of gangliotetraosylceramide. These findings are discussed in light of the hypothesis that NK cells interact with susceptible target cells through cell surface glycoconjugates. (Author abstract) (23 Refs)

### 29. THE FUNCTIONAL CHARACTERIZATION OF MALIGNANT LY 1+ T CELL CLONES ISOLATED FROM B CELL LYMPHOMAS (MEETING ABSTRACT)

Sing AP, Morgan N, Reinisch CL
Department of Comparative Medicine, Tufts University School of Veterinary Medicine, Boston, MA
Fed Proc; 41(3):478 1982

C57Bl/6 mice develop plasmacytoid lymphocytic lymphomas 2 years after injection with MSV-MuLV-Moloney. Cells from the mesenteric lymph node (MLN), unseparated spleen cells or splenic B cells injected into normal B6 mice proliferate in the MLN and spleen causing B cell lymphomas in 3-4 months. Cells from the lymphoma cell population were cloned at limiting dilution (0.3 cells/well) in the absence of TCGF on a syngeneic feeder layer to establish a series of clonally derived lines. Thus far, 8 clones, designated MSV-LN-AS 1-8 have been generated from individual MSV infected mice; when analyzed with monoclonal antibodies, the cells express the Ly1 and Thy 1.2 differentiation antigens. They are Ly2-, Qa2-and Ig-. Cells isolated from B6 mice injected with malignant lymphoma cells and cultured similarly are also Ly1+Ly2-Thy 1.2+Qa2-Ig-. As few as 1 x 10(6) Ly1+ T cells from the MSV-AS series injected into normal B6 mice cause immunoblastic T cell sarcomas which kill the recipient in one week. Functional characterization of one clone shows that the cells enhance IgM and IgG responses to SRBC in vivo, potentiate specific CTL reactivity to alloantigen in vivo and stimulate Ig secretion by B cells in vitro. These experiments show: 1) a series of Ly1+ T cell clones have been isolated from B cell lymphomas 2) the T cell clones are highly malignant and phenotypically identical and 3) the clones interact with B or T cells to potentiate immune responsiveness. (no Refs)

## CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION

### 30. ALTERATIONS IN THE PHENOTYPE OF HAIRY CELLS DURING CULTURE IN THE PRESENCE OF PHA: REQUIREMENT FOR T CELLS.

Worman CP, Beverley PC, Cawley JC
Dept. Haematology, Univ. Coll. Hosp., Grafton Way, London WC1, England
Blood; 59(5):895-899 1982

Culture studies of peripheral blood mononuclear cells from seven entirely typical cases of hairy cell leukemia showed that after culture in the presence of PHA for 2-5 days, the predominant cell type changed from E- SIg+ CIg+ gammaFcR+ muFcR+ hairy cells to an E+ SIg- CIg- gammaFcR- muFcR- population of transformed cells derived from hairy cells. Depletion and readdition experiments demonstrated that cell-to-cell contact with T cells was necessary for the phenotypic change, while several observations indicated that the E+ population was not derived from T cells present before culture. The E positivity of the cultured cells was shown to be due to the possession of E receptor not acquired from the culture fluid, but the cells differed from true T cells in lacking both mature and immature T-cell antigens. The relevance of these in vitro observations to the continuing controversy concerning the nature of the hairy cells and to the in vivo fluctuations in immunologic phenotype not infrequently observed in hairy cell leukemia is briefly discussed. (Author abstract) (23 Refs)

### 31. EFFECTS OF PHORBOL ESTER ON MYELOID-MONOCYTE SPECIFIC ANTIGENS IN HUMAN MYELOID LEUKEMIA CELLS (MEETING ABSTRACT)

Sugimoto T, Tatsumi E, Takeda K, Bloch A, Civin C, Minowada J
Roswell Park Memorial Institute, Buffalo, NY, 14263
Proc Am Assoc Cancer Res; 23:1087 1982

Using 5 monoclonal antibodies (MCS-1, MCS-2, 1/12/13, OKM-1, BRL-Mo) specific to human myeloid-monocyte surface antigens, changes in the antigen expression of leukemic myeloid/monocytes were studied by membrane immunofluorescence with phorbol ester-driven in vitro macrophage differentiation system. First, three myelocytic (ML-1, HL-60 and KG-1) and a monocytic (THP-1-0) leukemia cell lines were studied. After treatment with the inducer, the treated cells from all 4 cell lines differentiated toward macrophage-like cells by morphology, adherence to the culture vessel and phagocytic activity. Changes in the marker profiles of those treated cells from 'myeloid' to 'macrophage-like' feature were observed. Fresh myeloid leukemia cells from 10 patients with acute myeloid leukemia were next studied similarly in a short-term culture with/without phorbol ester. While considerable heterogeneity in the marker profiles was evident from case to case, we found (1) majority of AML (acute myeloid leukemia) cells share an antigen(s) in common with monocytes and (2) spontaneous differentiation of myeloblasts even without phorbol ester treatment takes place toward macrophage-like cells. The observed findings indicated that myeloid leukemias are heterogeneous in regard to their membrane phenotype having a bipotential differentiation capacity and that cellular origin between myeloid and monocytoid cells might be the same precursor. (no Refs)

### 32. INDUCTION OF DIFFERENTIATION OF HL-60 LEUKEMIC CELLS BY POST-ENDOTOXIN SERUM (MEETING ABSTRACT)

Chiao JW, Bressler J, Pinsky C, Hirshaut Y, Oettgen HF, Clarkson B
Sloan-Kettering Institute for Cancer Research, New York, NY, 10021
Proc Am Assoc Cancer Res; 23:893 1982

Serum from cancer patients treated with endotoxin was tested for activity for induction of differentiation of leukemic cells in vitro. Liquid cultures of HL-60 human leukemic promyelocytes were supplemented with 20% pre- or post-endotoxin serum from patients with melanoma or ovarian carcinoma injected with endotoxin. Cultures supplemented with post-endotoxin sera showed a significant increase in the number of cells with membrane complement receptors, markers for differentiation. This did not occur in control cultures incubated with pre-injection serum from the same individual. Approximately 7.5% of the cells cultured with post-endotoxins sera displayed complement receptors after three days, compared to none in the initial cultures and in three day control cultures. The proportion of cells with complement receptors reached a peak on day five with a mean of 12.5% and a range of 5-29%. The increase in the absolute number of cells with complement receptors was much higher than the increase in total cell number which suggests that the presence of these cells was due to differentiation rather than selective proliferation or cell death. In-

duction of differentiation was mediated by serum collected 2-12 hours after injection of endotoxin. Incorporation of 3H-thymidine into replicating cells was tested as a measure of proliferation of HL-60 cells during induced differentiation. A decrease in proliferation was evident in cultures supplemented with post-endotoxin serum. This decrease always preceded the appearance of complement receptor bearing cells. (no Refs)

## 33. QUANTITATION AND MODULATION OF IA ANTIGENS ON CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) CELLS (MEETING ABSTRACT)

Okamura J, Letarte M, Gelfand EW
Hospital for Sick Children, Toronto, Ontario, M5G 1X8, Canada
Proc Am Assoc Cancer Res; 23:1066 1982

To investigate the possible correlation between quantitative expression of Ia antigens and B cell differentiation, we measured the amount of Ia on CLL cells using a cellular radioimmunoassay. Five x 10(5) CLL cells were incubated with 21w4, a monoclonal anti-Ia antibody, prior to incubation with saturating amounts (500 ng) of 125I-F(ab')2 rabbit anti-mouse IgG-Fc (RAM-Fc). The relative amount of Ia is expressed in ng of RAM-Fc bound per 5x10(5) CLL cells. In 10 CLL patients studied, the amount of surface Ia was shown to be heterogenous, varying from 13 ng to 107 ng. Following culture with 12-tetradecanoylphorbol 13-acetate for 1 to 3 days, the amount of Ia on CLL cells increased over resting levels in all patients. In 6/8 patients, the amount of Ia was significantly elevated by day 1. In 5/6 patients in this group, staining of CLL cells for cytoplasmic immunoglobulin (cIg) became positive. Low mean cell volume (less than 166fL) and low amounts of Ia (less than 60 ng) were additional characteristics of the cells from these 5 patients. These TPA-induced changes were also associated with an increase in cell volume and enhancement of stimulatory capacity in mixed lymphocytic reaction (MLR). Our results indicate that there may be stages of B-cell differentiation at which cells express large amounts of Ia, cIg and stimulate well in MLR. Modulation of CLL cells by TPA thus provides a new approach to the characterization of stages in B cell ontogeny. (no Refs)

## 34. DIFFERENTIATION OF K-562 CELLS: INDUCTION BY THYMOSIN FRACTION 5 (MEETING ABSTRACT)

Ichiki AT, Lozzio BB, Lozzio CB, Bamberger EG
University of Tennessee Center for the Health Sciences, Knoxville, TN, 37920
Fed Proc; 41(3):795 1982

K-562 cells differentiate along the erythrocytic, granulocytic, and monocytic series; hence K-562 cells are considered to be multipotential leukemic cells. These cells express both specific leukemia associated antigens (LAA) and Fc receptors. We initiated a study employing monoclonal antibody preparations to determine the presence of other surface membrane antigens on the K-562 cells. When evaluated with the Cytofluorograf for the binding of F(ab')2 fragment of goat anti-mouse IgG, K-562 cells from 6 or 7 day-old cultures did not bind anti-HLA-A,B,C, anti-HLA-DR, OKT10 (reactive with thymocytes, BM terminal transferase positive cells, BM precursor B cells, and myeloblasts), OKT11 (reactive with large thymic blasts), or anti-monocyte antibody. Over 90% of the cells bound the five monoclonal anti-K-562 antibody preparations of differing specificities. The incubation of cells with thymosin fraction 5 for 24 hours led to changes in the expression of some surface antigens. The number of HLA-A,B,C expressing cells was increased but the number of OKT10 binding cells was only noticeably increased. There was also an increased intensity of the expression of LAA. The fact that the incubation of the K-562 cells with thymosin fraction 5 resulted in the expression of HLA-A,B,C suggests that these cells could be induced to differentiate along the lymphocytic series. (no Refs)

## 35. CHANGES IN GLYCOSIDASE ACTIVITIES AND SURFACE LECTIN RECEPTORS OF GUINEA-PIG ALVEOLAR MACROPHAGES ACTIVATED BY CORYNEBACTERIUM PARVUM.

Blanquet PR, Scharfman A, Aerts C, Roussel P, Biserte G
Institut de Recherches sur le Cancer et Unite 124, I.N.S.E.R.M., 59020 Lille Cedex, France
Cell Mol Biol; 28(1):111-118 1982

This report deals with the activity of five selected glycosidases and the topographic distribution of surface receptors of peroxidase-postlabeled Con A and four peroxidase-conjugated lectins in normal and Corynebacterium parvum-induced alveolar macrophages derived from guinea-pigs. It is shown that a striking rise in the activity of N-acetyl-beta-D-glucosaminidase, N-acetyl-beta-D-galactosaminidase, beta-D-glucuronidase and beta-D-galactosidase is paralleled by a more regular distribution of surface-bound wheat germ agglutinin in C parvum-induced cells. In contrast, the activity of alpha-D-mannosidase shows no increase; likewise, no apparent difference in surface staining patterns of Con A, soybean and Ricinus communis agglutinins is noted. (Author abstract) (26 Refs)

## 36. CHEMOTAXIS OF GRANULAR LEUKOCYTE: ITS BIOCHEMICAL AND MORPHOLOGICAL MECHANISM.

Hirashima M, Hirotu Y, Hayashi H
First Dept. Pathology, Kumamoto Univ. Sch. Medicine, Kumamoto, Japan
Nippon Rinsho; 39(8):2701-2708 1981

Two neutrophil chemotactic factors (NCF) are known: the primary factor leucoegresin (mol wt 140,000) and the secondary factor (mol wt 14,000) a derivative of C5. Both are thermoresistant. Artificial peptides, such as f-Met-leu-phe, also serve as NCF. Others were also found, but were thought to be less important. Eosinophilic chemotactic factor (ECF) consists mainly of thermolabile early factor (mol wt 500) and thermolabile delayed factor (mol wt 70,000). The early factor may be the ECF-A (ECF of anaphylaxis) or a similar molecule. The delayed factor can be further separated into two different antigens: a and b. Various other factors were also found. All basophilic chemotactic factors studied so far are the results of the in vitro experiments, and no studies have yet been performed with a natural mediator. The two types of leukocyte movement are the random movement occurring in a medium without concentration gradient of the chemotactic factors (CF), and the directional chemotactic movement that initiates the gradient of CF concentration. The latter movement is initiated when CF binds CF receptors on the membrane to form lamellipodium as the forward section. The binding of CF to the CF receptor triggers several biochemical reactions, acting on microfilaments and microtubules, which are moved around within the cell due to gradient changes of Ca++ and Na+. (45 Refs) (In JPN)

## EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS

### 37. INHIBITORY EFFECTS OF VARIOUS OXYGENATED STEROLS ON THE DIFFERENTIATION AND FUNCTION OF TUMOR-SPECIFIC CYTOTOXIC T LYMPHOCYTES.

Spangrude GJ, Sherris D, Daynes RA
(c/o Daynes) Dept. Pathology, Univ. Utah Medical Center, Salt Lake City, Utah, 84132
Transplantation; 33(5):482-491 1982

These studies were undertaken to determine the effect of various oxygenated sterols (representing a number of known cholesterol-derived photoproducts) on the generation (afferent) and function (efferent) of cytotoxic T lymphocytes (CTLs). Cell-mediated immune responses which result in the generation of both alloantigen-specific and syngeneic tumor-specific CTLs were evaluated. The results of our studies established the following points: (1) the afferent phase of an immune response is particularly sensitive to the effects of some cholesterol photoproducts while other oxidized sterol derivatives, known to exist in skin following UV light (UVL) exposure, have minimal influence on the generation of CTL responses; (2) the only known carcinogenic photoproduct of cholesterol (cholesterol alpha-oxide) is a very weak inhibitor of lymphocyte function; and (3) presentation of oxygenated sterols via liposome membranes is 10-fold more effective than their administration in soluble form; (4) 25-hydroxycholesterol and 20alpha-hydroxycholesterol were found to be the most potent inhibitors, causing a parallel depression in lymphocyte proliferation, CTL activity, and endogenous sterol biosynthesis, and (5) 7beta- and 7alpha-hydroxycholesterol functioned in a unique manner, causing an abrogation of CTL activity without depressing proliferative responses and endogenous sterol biosynthesis to a significant degree. These studies represent the first time that an attempt has been made to evaluate a possible biochemical basis for immune suppression known to precede experimental UVL carcinogenesis. Our results suggest that some, but not all, of the oxidation products of cholesterol found in skin following UVL irradiation exert an influence on immune responses. Derivatives of cholesterol could be partially responsible for the alterations in immunological potential of the UVL-exposed host. The induced presence of an inhibitor of CTL differentiation or function at a time following UVL tumor emergence may play a role in this process by providing an early tumor escape mechanism. (37 Refs)

### 38. CHARACTERIZATION AND DRUG TREATMENT OF HUMAN LYMPHOCYTES IN A COLONY ASSAY (MEETING ABSTRACT)

Mendelsohn J, To D, Taetle R
Department of Medicine, University of California San Diego Cancer Center, La Jolla, CA, 92093
Proc Am Soc Clin Oncol; 1:C-167 1982

Human peripheral blood lymphocyte subpopulations were cultured in 1% methyl cellulose with irradiated mononuclear cells and 20% medium conditioned by PHA (phytohemagglutinin)-stimulated normal T cells. Colonies of greater than 50 cells were scored after 5-7 days. Subpopulations studied included fresh E+ (T) cells, PHA stimulated (cycling) E+ cells, E- cells (T cell depleted) and B-CLL (B-chronic lymphocytic leukemia) cells. Each grew with linear plating characteristics over a range of nearly 1 log. Phenotyping of colonies for surface markers showed predominant proliferation of the subpopulation plated. The percent of colony forming cells (CFC) in S phase (determined by TdR (thymidine) suicide) was similar in the normal subpopulations, ranging from 24 to 33%. Fresh and PHA-stimulated E+ CFC had similar sensitivities to both S phase active and non-phase specific drugs, similar plating efficiencies, and similar high TdR suicide values, suggesting that CFC may be a minor, distinct, cycling subpopulation. Adriamycin was uniquely less toxic to fresh than to stimulated E+ CFC exposed for 1 hr, but was equitoxic with continuous exposure, possibly suggesting slower uptake by fresh E+ cells. The stimulated E+ CFC were more sensitive to steroid sex hormones, but not to cortisol, at concentrations greater than 10 uM. In contrast with E+ CFC, B-CLL CFC from different donors showed a wide variation in susceptibility to killing by drugs and hormones. This culture system permits comparative studies of resting and cycling lymphocytes, and of normal and malignant lymphocyte subpopulations. (no Refs)

### 39. LYCURIM (R-74) IN THE THERAPY OF CHRONIC LYMPHOCYTIC LEUKAEMIA.

Vygovskaya YI, Loginsky VE, Vorobel AV, Kondratieva NA, Mazurok AA, Korotky VV, Kotsay BR
Res. Inst. Heamatology and Blood Transfusion, Pushkin St. 45, 290044 Lvov, USSR
Haematologia (Budap); 14(4):399-405 1981

Clinical and hematologic effects of Lycurim (R-74) were studied in 41 patients with chronic lymphocytic leukemia (CLL) and influence of R-74 on cellular and humoral immunity is described. R-74 was administered iv in doses of 30-60 mg/day in courses of 120-1470 mg depending on individual sensitivity. During R-74 therapy the dose of corticosteriods was decreased. Twenty-five patients showed marked improvement immediately after treatment, displaying a normal body temperature, decrease of perspiration, improvement of appetite, and increase of body wt. The WBC count of 14 patients decreased from 282.1 +-58.2 x 10(9)/liter (l) to 60.5 +-18.7 x 10(9)/l. Patients who received smaller doses of R-74 showed a WBC decrease from 75.0 +-16.8 x 10(9)/l to 23.2 +-8.7 x 10(9)/l. Somatic compensation after treatment constituted a period of 7-14 mo for 16 patients, 4-6 mo for 7, and 1-3 mo for 5. Three CLL patients after R-74 treatment underwent splenectomy which prevented the evaluation of after-effects. Four patients did not report for hematologic control. Thirty-one CLL patients were studied for immune status prior to and immediately after R-47 treatment. Marked changes in the immunological indices were observed. The results of agar gel electrophoresis showed a definite decrease of the beta2 and gamma-globuulin fractions to 2.3 +-0.2 g/l and 12.5 +-1.3 g/l, respectively. CLL patients showed a definite increase of the B-lymphocyte content which have surface markers for Ig and C3 to 48.5 +-2.7%. This increase occured as a result of an accumulation of leukemic B-lymphocyte population of monoclonal origin in peripheral blood. Results showed that R-74 treatment results in a definite antitumoral and immunodepressive effect. (8 Refs)

### 40. IDENTIFICATION BY MONOCLONAL ANTIBODIES OF T CELL SUBPOPULATIONS ACTIVATED BY 12-O-TETRADECANOYL-PHORBOL-13-ACETATE (TPA) (MEETING ABSTRACT)

Kaplan JH, Lee LS, Lockwood SH
General Electric Corporate Research and Development, Schenectady, NY, 12301
Proc Am Assoc Cancer Res; 23:1054 1982

Two major T cell subpopulations identified by their reactivity to the monoclonal antibodies OKT4 and OKT8 were stud-

ied for their capacity to be activated by the tumor promoting agent TPA. To obtain T cells that did not have Fc receptors for IgG, mononuclear cells isolated from human peripheral blood by centrifugation on a Ficoll-Hypaque gradient, and then depleted of monocytes, were placed on an immunoadsorbent column of human Ig-rabbit IgG anti-human Ig. The cell fraction that did not adhere was comprised of greater than 85% T cells and only 0.1% B cells. Sixty-two percent of these T cells possessed T4 surface antigen while 23% comprising another subset were shown to carry on their surface T8 antigen. Negative selection procedures by complement-dependent lysis were used to separate T4+ from T8+ cells. The fraction enriched in T8+ cells showed approximately a 1.2-2.0 fold greater mitogenic response to TPA (20 ng/ml) than did the T4+ cell subset. Optimal activation by TPA required the presence of monocytes. Comparison of the summed mitotic activity of each T cell subset was less than a mixture of the two. (no Refs)

## 41. INTERFERON INCREASES HLA SYNTHESIS IN MELANOMA CELLS: INTERFERON-RESISTANT AND -SENSITIVE CELL LINES.

**Basham TY, Bourgeade MF, Creasey AA, Merigan TC**
**Div. Infectious Diseases, Dept. Medicine, Stanford Univ. Sch. Medicine, Stanford, CA, 94305**
**Proc Natl Acad Sci USA; 79(10,part1):3265-3269 1982**

We report that human leukocyte interferon preparations increase the expression of beta2-microglobulin by 100-200% on the surface of normal fibroblast and melanoma cell lines sensitive to interferon. This increase in expression can be correlated with an increase in HLA synthesis as measured by incorporation of [35S]methionine in these antigens. This enhanced HLA synthesis, which is 5-to 17-fold, is time dependent and dose related. Synchronized cells in the G0/G1 phase of the cell cycle appear to be more sensitive to this interferon action. Neither an increase in surface expression nor in HLA synthesis is observed in a melanoma cell line resistant to the antiviral and antigrowth effects of interferon. Furthermore, there appears to be a stronger correlation between this increased HLA synthesis and the antiviral function than between it and the antiproliferative action of interferon. (Author abstract) (18 Refs)

## 42. ACTIVATION OF NK CYTOTOXICITY IN CANCER PATIENTS TREATED WITH INTERFERON OR INTRALESIONAL BCG (MEETING ABSTRACT)

**Golub SH**
**Department of Surgery, University of California Los Angeles School of Medicine, Los Angeles, CA**
**9th International RES Congress, February 7-12, 1982, Davos, Switzerland. American Reticuloendothelial Society 68 pp., 1982.**

Natural killer (NK) activity aganist K562 targets was examined with lymphocytes from melanoma patients treated with human leukocyte interferon (IFN) and from patients with various types of tumors treated with intralesional BCG. IFN treatment was regularly associated with increased NK cytotoxicity of peripheral blood lymphocytes (PBL) during the first week of treatment, with peak activity at 7 days of treatment. Subsequently, NK declined towards pre-treatment levels despite continued IFN administration. The early period of increased NK was associated with increased numbers of both target binding and target killing cells as determined by the single cell agarose assay. The period of declining NK was concurrent with an inability to boost in vitro PBL NK activity with IFN. In vitro responsiveness to IFN could not be restored by removal of adherent cells, but promptly returned when the patients ceased receiving IFN in vivo. NK cells throughout the course of treatment retained the usual NK characteristics of Fc receptors and nylon non-adherence. Intralesional BCG also augmented NK activity with increased cytotoxicity detectable in PBL, draining lymph node lymphocytes, and in the lymphocytes infiltrating the BCG-injected tumor site. However, low NK activity was found among lymphocytes infiltrating uninjected tumor sites in patients where injected tumors had high NK. Results in both IFN and BCG systems indicate that systemic NK activity can be augmented but that it is difficult to maintain NK activity at elevated levels or to deliver these cells to tumor sites. (no Refs)

## 43. POLY-I-C BOOSTS A NATURAL KILLER CELL POPULATION WHICH KILLS SOLID TUMORS (MEETING ABSTRACT)

**Lattime EC, Pecoraro GA, Cuttito M, Stutman O**
**Memorial Sloan-Kettering Cancer Center, New York, NY, 10021**
**Proc Am Assoc Cancer Res; 23:956 1982**

Natural cell mediated cytotoxicity (NCMC) is a function of at least two distinct effector cell populations, natural killer (NK) and natural cytotoxic (NC). The two cells differ in cell surface antigen expression (NK cells are Qa-5+, Asialo-GM-1+; NC cells are Qa-5-, ASGM-1-), and their activities can thus be separated by antibody and C' mediated elimination. Early studies have shown that NK cells preferentially kill lymphoid tumors while NC cells kill solid tumors. A number of solid and lymphoid tumors were examined for their susceptibility to killing by NC and NK cells using long term (18 hr) 51Cr release assays and effector cells from untreated and poly-I-C (10 ug/mouse ip) boosted mice. The tumors studied can be divided into three categories according to their susceptibility to NC and NK cell killing: 1) NK susceptible, all lysis is a function of an NK effector cell in both untreated and poly-I-C treated mice (YAC-1, L-5178 cl 27v, CMS-2, Meth-Z); 2) NC and NK susceptible, sensitive to killing by both effectors, with the NK component increased in poly-I-C treated animals (Meth-X, Meth-E4, UV-2237, CMS-4); and 3) NC susceptible, all lysis is due to NC activity which is not increased by poly-I-C treatment (Meth-A, Meth-A.N, WEHI-164.1). These studies demonstrate that depending on the state of activation of the effector cell population, solid tumors are differentially sensitive to lysis by NC and NK cells. (no Refs)

## 44. CHARACTERIZATION OF REMISSION LYMPHOCYTES CYTOTOXIC TO AUTOLOGOUS LEUKEMIA CELL AFTER TREATMENT WITH POLY AU AND LEVAMISOLE (MEETING ABSTRACT)

**Sharma BS**
**University of California, Irvine, CA, 92717**
**Fed Proc; 41(3):602 1982**

Remission lymphocytes (RL) from pediatric leukemia patients cytotoxic to leukemia cells (LC) after treatment (TM) with poly AU and levamisole, synthetic immunomodulators (SIM) were characterized. RL were isolated by Ficoll-Hypaque and fractionated. Unfractionated (UF) and various cell fractions were treated and cytotoxicity (CY) was tested to 51Cr-LC. The results are: 1) when SCMC was high, culturing of RL alone (CC) caused loss of CY, but TM with SIM induced CY and suppressed when CC was high, 2) precursors (P) of induced RL were usually nylon wool nonadherent cells and NW-adherent in some cases, 3) TM of RL with high SCMC resulted in negative CY, but after depletion of NW-A cells and TM induced CY, suggesting the induction of suppressor cells or an immunoregulator, 4) SIM including cytoxan in-

duced or did not induce CY against LC, indicating SIM may modulate CMC through same pathway, may be via induction of interferon, 5) P of induced effectors were in T, non T, FcR+ and FcR- cell fractions. F of induced effectors were non-EAC RFC (erythrocyte antibody compliment-rosette forming cell), 6) induced cells were lytic to LC, but not to autologous RL, and 7) induced cells were lytic to some but not to all LC. This study demonstrates that TM of RL with SIM induced killer lymphocytes with characteristics similar to NK or NK-like cells. (no Refs)

### 45. CELLULAR INTERACTIONS IN VITRO IN A PRIMARY ANTI-TUMOR RESPONSE.

Levy JP, Gomard E, Wibler-Franqui J, Herberman RB, Chang KS, Aoki T, Hashimoto Y
Laboratoire d'Immunologie et de Virologie des Tumeurs, Hopital Cochin, Paris, France
Excerpta Med Int Congr Ser; 576:268-281 1981

Factors affecting generation of mouse spleen cytotoxic T lymphocytes (CTL) against tumor cells carrying a virus-induced antigen closely related to the serologically defined FMR system (anti-FMR CTL) were investigated. Cytotoxicity was determined by 51Cr release. In vitro generation of primary anti-FMR CTL appeared to require the presence of a radioresistant, adherent, phagocytic, Thy 1-2-negative cell, probably a macrophage. These macrophages interacted with T cells because of Ia specificities. CTL activity was directed by the tumor cell H-2 specificity. This requirement for macrophages could be replaced by interleukin 2 (IL2), suggesting that macrophages may trigger IL2 production by presenting an Ia+ antigen to an anti-FMR helper T cell. Further work showed that Thy1-2 (+) primed helper T cells in the presence of normal macrophages triggered anti-FMR CTL from normal thymocytes. Lentinan (1 mg/kg days-7 to-2) increased CTL production, but not consistently. Other work suggests that Lentinan may increase the sensitivity of precursor CTL to IL2. (19 Refs)

### 46. THE STATE OF SYMPATHOADRENAL SYSTEM AND IMMUNOLOGIC RESPONSE IN CANCER PATIENTS.

Filatova NA, Sheveleva VS, Mel'nikov RA, Simonov NN, Gorlanov IA
N. N. Petrov Res. Inst. Oncology, USSR Ministry Health, Leningrad, USSR
Vopr Onkol; 28(2):80-84 1982

The study is concerned with the rosette-forming reaction of T- and B-lymphocytes of peripheral blood and their activity in blast transformation reaction to phytohemagglutinin in patients with carcinoma of the stomach, colon, rectum and breast. A clinical assessment was made before and after a 10-day administration of a complex preparation stimulating the activity of vegetative centers and promoting redox processes in tissues. The treatment improved the tone of the sympathoadrenal system and immunologic response in cancer patients. (Author abstract) (13 Refs) (In RUS)

### 47. ROLE OF HOST AND DONOR CELLS IN TUMOR ELIMINATION FOLLOWING ADOPTIVE CHEMOIMMUNOTHERAPY (ACIT) (MEETING ABSTRACT)

Greenberg PD, Cheever MA, Fefer A
University of Washington and Hutchinson Cancer Research Center, Seattle, WA, 98195
Proc Am Assoc Cancer Res; 23:1014 1982

The purpose of these studies was to define the relative contributions of host and donor cells to the eradication of disseminated FBL erythroleukemia in C57BL/6 mice by curative ACIT with cyclophosphamide (CY) and syngeneic lymphocytes. Previous studies, demonstrating that tumor elimination occurs over several weeks and requires transfer of specifically immune noncytolytic Lyt 1+2-T cells (rather than donor CTL) underscore the potential for a host contribution and donor-host interactions. The roles of host and donor cells have been analyzed by using host and donor mice congenic for genes encoding for T cell antigens, and by modulating host or donor T cells after therapy by inoculating high titer monoclonal IgG antibodies to the allelic T cell antigens. C57BL/6 mice bearing FBL tumor were curatively treated with CY plus 2 X 10(7) immune spleen cells obtained from either immune C57BL/6 mice (Thy 1.2) or congenic B6.PL/Thy 1.1 donor mice (Thy 1.1). After 60 days, mice receiving congenic cells appeared tumor-free, showed no graft-vs-host disease, had no serum antibody to either Thy antigen, and were sacrified to determine the origin of splenic T cells. Although only a minor fraction of naive alloreactive splenic T cells were of donor origin, donor T cells comprised the majority of cells reactive to tumor. Inoculation of lytic monoclonal IgG antibodies to Thy 1.1 rapidly depleted spleens in vivo of both naive and tumor-immune Thy 1.1 cells. (no Refs)

### 48. IN VITRO AND IN VIVO EFFECTS OF A SUGAR DERIVATIVE OF NITROSOUREA (RFCNU) ON IMMUNE RESPONSE IN THE CANCER PATIENT.

Cupissol D, Rey A, Favier F, Serrou B
Laboratoire d'Immunopharmacologie des Tumeurs, INSERM U-236, ERA-CNRS No. 844, Centre Paul Lamarque, BP 5054, 34033 Montpellier Cedex, France
INSERM Symp; 19:221-228 1981

(Chloro-2-ethyl)-1-(ribofuranosyl-isopropylene-2'-3' paranitrobenzoate-5')-3 nitrosourea (RFCNU) was tested in in vitro studies with lymphocytes and in in vivo studies with patients with either epidermoid lung cancer or digestive tract tumor accompanied by liver or lung metastases. RFCNU is not immunodepressive for the patient as judged by delayed hypersensitivity, auto-rosette levels, and natural killer activity. The drug had low myelotoxicity and was well tolerated even though treatment times were extended due to thrombocytopenia in 30% of the cases. (12 Refs)

## OTHER RELATED STUDIES

### 49. IMMUNOGLOBULIN HEAVY CHAIN GENE REARRANGEMENT AND TRANSCRIPTION IN MURINE T CELL HYBRIDS AND T LYMPHOMAS.

Zuniga MC, D'Eustachio P, Ruddle NH
(c/o Ruddle) Dept. Epidemiology and Public Health, Yale Univ. Sch. Medicine, 60 College St., New Haven, CT, 06510
Proc Natl Acad Sci USA; 79(9):3015-3019 1982

We have examined the arrangement of immunoglobulin heavy chain constant (CH) and joining (JH) region genes in murine T cell hybrid lines and in T lymphomas. CH genes derived from both parental cell types were present in all hybrids for which polymorphism in sequences flanking CH genes permitted us to distinguish parental CH genes. All T lymphomas and T cell hybrids retained the Calpha gene in germ-line configuration and all but one cell line had germ-line Cmu genes. Novel DNA fragments reactive with JH probes were observed in six of nine T cell hybrids, as well as in two T lymphomas,

WEH17.1 and YAC-1, but not in the fusion parent, BW5147. No RNA homologous to Cgamma2b, Calpha, or lambda genes was detected in any of the T cell lines. T cell lines contained poly(A)+ RNA homologous to a Cmu cDNA probe. More importantly, in several cell lines the Cmu RNAs were associated with membrane-bound polyribosomes. These results suggest that both JH rearrangements and Cmu RNA production occur in at least some mature, antigen-specific T cells. They may therefore reflect events in normal T cell development and function related to those involved in the generation of the T receptor for antigen. (Author abstract) (30 Refs)

## 50. MECHANISMS OF IMMUNITY IN CANCER.

Baldwin RW
Cancer Res. Campaign Lab., Univ. Nottingham, Nottingham NG7 2RD, England
Pathobiol Annu; 11:155-175 1981

Immunological recognition of malignant cells in human tumors, malignant melanomas, and other tumors, and the role of suppressor T cells and other suppressor factors are discussed. The tumor cell must express an appropriate tumor associated antigen for a tumor to generate specific T lymphocyte response and/or initiate antibody formation. Original evidence cited in identifying human tumor associated antigens showed that peripheral blood lymphocytes from patients were cytotoxic in vitro when tested on cultured tumor cells, reactivities indicating that many tumors exhibited tumor-type specific antigens. The reactivity of monoclonal antibody (MCAB) produced by two hybridoma lines prepared against human osteogenic sarcoma cell line is presented. Production of MCAB to melanoma associated antigens by hybridomas derived from fusion of mouse myeloma cells and spleen cells from mice immunized with cultured melanoma cells or membrane fractions was observed. The antibody preparation reacted strongly with cells of the immunizing melanoma and less strongly with an allogeneic melanoma. MCAB specifying cell surface antigens have been produced against other human tumors, including carcinomas of the colon, neuroblastoma, and leukemic cells. MCAB are being produced against a number of tumor associated substances, including carcinoembryonic antigen, human alpha-fetoprotein, and human fibrinolectin. Virus related antigens upon tumor cells, such as Epstein Barr virus antigens, also can be detected by MCAB reagents. Adoptive transfer experiments also have been used to demonstrate a requirement for specifically sensitized T lymphocytes in tumor rejection. One of the most significant aspects of T lymphocyte recognition of tumor associated antigens is the finding that T suppressor cells rather than T cells mediating tumor rejection may be induced. (102 Refs)

## 51. MURINE MONOCLONAL ANTIBODY THERAPY IN TWO PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA.

Dillman RO, Shawler DL, Sobol RE, Collins HA, Beauregard JC, Wormsley SB, Royston I
Hematology/Oncology Section (111E), Univ. California, Veterans Admin. Hosp., 3350 La Jolla Village Drive, San Diego, CA, 92161
Blood; 59(5):1036-1045 1982

We infused the murine monoclonal antibody T101 into two patients with advanced refractory chronic lymphocytic leukemia (CLL) after confirming its reactivity with their CLL cells. One patient received doses of 1, 3, and 12 mg; the second patient received 10 mg. Antibody was delivered over 10-15 min. The major observations were: (1) T101 murine monoclonal antibody did bind to cells with T65 surface antigen and saturated these cells in vivo; (2) cells that bound T101 disappeared from the circulation by 2 hr after treatment, as evidenced by a marked drop in lymphocyte counts; (3) T101 serotherapy resulted in some intravascular cell injury associated with sequestration and probably destruction in the liver and lung; (4) free serum T101 was demonstrable, but disappeared by 2-4 hr after infusion; (5) rapid infusion of T101 did not induce significant modulation of T65; (6) rapid infusion of greater than 10 mg of T101 was associated with significant systemic reactions. Monoclonal antibodies may someday have an application in leukemia therapy, but additional experimental trials are clearly indicated. (Author abstract) (26 Refs)

## 52. IN VITRO PRODUCTION OF TUMOR-RELATED HUMAN MONOCLONAL ANTIBODY AND ITS IMMUNOHISTOCHEMICAL SCREENING WITH AUTOLOGOUS TISSUE.

Hirohashi S, Shimosato Y, Ino Y
Pathology Div., Natl. Cancer Center Res. Inst., 1-1, Tsukiji 5-chome, Chuo-ku, Tokyo 104, Japan
Gan; 73(2):345-347 1982

The property of Epstein-Barr virus (EBV) to transform human B lymphocytes into lymphoblastoid cells secreting immunoglobulins was used to obtain human antibodies against human tumors. EBV was taken from the marmoset cell line B95-8. A virus stock was produced by culturing B95-8 cells for 7 days in a medium of RPMI-1640 supplemented with 20% heat inactivated fetal bovine serum, 100 Units/ml penicillin, and 100 ug/ml streptomycin, separating culture supernatants, and filtering through a Millipore filter. Regional lymph nodes were obtained at surgery from a 45-yr-old woman with Dukes' C moderately-differentiated adenocarcinoma of the rectum and from a 37-yr-old man with Borrmann's Type II signet ring cell carcinoma of the stomach. Single cell suspensions were prepared from the lymph nodes, resuspended in culture medium, and then mixed with virus stock. A 0.1 ml portion of the resulting mixture was distributed to 92-well tissue culture plates, cultured for 4 wk, and transferred to 24 other well tissue culture plates for 2 more wk of culturing. Culture supernatants were harvested and screened for the presence of antibody against autologous tumor tissue. In the case of rectal cancer, supernatants from 6/24 well positively stained the autologous tissue. The reaction products were located at the luminal surface of tumor cells, and the distribution was quite similar to that of carcinoembryonic antigen. In the case of gastric cancer, supernatants from 7/24 wells positively stained the autologous tissue. The results demonstrate that human antibodies against human tumors and normal tissues can be produced by EBV transformation of lymphocytes, suggesting that there is potential clinical application of this technique for treating tumors and that lymphocytes producing autoantibodies against normal tissues could be easily cultured from the lymph nodes adjacent to tumors. (6 Refs)

## 53. CHARACTERIZATION OF MURINE IFN-Y PRODUCING T-CELL LYMPHOMAS (MEETING ABSTRACT)

Landolfo S, Sarzotti M, Cavallo G, Arnold B
Institute of Microbiology, 10126 Torino, Italy
Fed Proc; 41(3):318 1982

Several established lines of murine T-cell hybrids and lymphomas were evaluated for their ability to produce interferon (IFN). Five clones derived from a T-cell lymphoma (L12) spontaneously grown in vitro and T cell hybrid, B9.1, derived from phosphorylcoline sensitized T-cells, were capable of pro-

ducing IFN when induced with mitogens such as phorbol myristic acetate (PMA), Con A (concanavalin A) or PHA (phytohemagglutinin). In addition all these tumor lines did not produce IFN either constitutively or upon LPS stimulation. Maximal IFN production (2,000 IU) was observed with PMA (2 x 10(-7) M), while Con A and PHA induction of IFN was found to be at intermediate levels (243 IU). The IFN produced by L12 cells was characterized as immune (y) being labile at pH2, neutralized by two different rabbit anti-murine antisera, but not by an antiserum to murine IFN-alpha and -beta. Phenotypic characterization revealed the producer cells to be Thy 1+, Lyt 1+, Lyt 2-3-, Ig-. These data established a useful and reproducible model for the purification and characterization of the molecular mechanisms involved in IFN-y production. (no Refs)

## 54. ACCESSORY CELLS IN THE IN VITRO GENERATION OF TYPE C VIRUS-SPECIFIC T-KILLER LYMPHOCYTES. III. TWO METHODS OF ANTIGEN PRESENTATION TO CYTOLYTIC T-LYMPHOCYTE PRECURSORS.

**Wybier-Franqui J, Gomard E, Levy JP**
**Laborstoire Immunologie et Virologie de Tumeurs, INSERUM U 152, CNRS ERA 781, Hopital Cochin, 75674 Paris Cedex 14, France**
**Cell Immunol; 68(2):287-301 1982**

F1 hybrid mice primed in vivo with tumor cells bearing the virus-induced FMR antigen and the H-2 specificities of each parent are able to produce in vitro in secondary response cytolytic T lymphocytes (CTL) reacting with FMR in the context of the H-2 antigens of both parents. This suggests that the processing in vivo of the immunizing cells by F1 macrophages results in the presentation of FMR antigens in the context of both H-2 specificities. It has also been suggested that FMR antigens are recognized by cytolytic T-lymphocyte precursors (CTL-P) at the surface of tumor cells and not of macrophages. The results reported here show that there are two methods of CTL-P priming: (a) in most cases, FMR antigens are presented directly by the tumor cells; (b) however, in the absence of antigen-presenting tumor cells in vivo or in vitro, macrophages present FMR to CTL-P. The presentation by macrophages appears less efficient but is probably sufficient to explain the priming of memory cells corresponding to both parental H-2. (Author abstract) (17 Refs)

## 55. CYTOPLASMIC INCLUSIONS IN LYMPHOCYTES OF CHRONIC LYMPHOCYTIC LEUKAEMIA. A REPORT OF 10 CASES.

**Raifkiaer E, Hou-Jensen K, Geisler C, Plesner T, Henschel A, Hansen MM**
**Dept. Pathology, Finsen Inst., DK-2100 Copenhagen, Denmark**
**Virchows Arch [Pathol Anat]; 395(2):227-236 1982**

Peripheral blood from 90 CLL patients was examined by light- and electron-microscopy for the occurrence of crystalline inclusions in lymphocytes. Inclusions were demonstrated in 10 patients (11%). In these patients the inclusions were present in 5-45% of peripheral blood lymphocytes. In the light microscope the inclusions appeared as rectangular, unstained structures in May-Grunewald Giemsa and PAS stains. In the electron microscope the inclusions appeared as intracytoplasmic, completely partially membrane-bound bodies, which were often associated with dilated profiles of rough endoplasmic reticulum. The ultrastructure of the inclusions was granular. In immunofluorescence staining the inclusions were found to contain immunoglobulin of the same type and class as the surface membrane-bound immunoglobulin of the neoplastic lymphocytes, most frequently IgM-lambda. The lymphocytes of one case with kappa light chains at the cell surface membrane contained inclusions of the same ultrastructural morphology as those of the other cases with lambda light chains. The presence of inclusions was not associated with any specific clinical or prognostic features. The inclusions persisted during antileukemic therapy. Their formation may be related to a dysfunction in the synthesis of surface membrane-bound immunoglobulins. (Author abstract) (29 Refs)

## 56. INTERMEDIATE FILAMENT BUNDLES IN HUMAN T LYMPHOCYTES IN MALIGNANT AND BENIGN SKIN DISEASES (MEETING ABSTRACT)

**McNutt NS**
**Departments of Pathology and Dermatology, University of California and Veterans Administration Medical Center, San Francisco, CA**
**Lab Invest; 46(1):55A 1982**

Intermediate filaments (IF) are cytoplasmic protein filaments, 10 nm diameter, which are part of the cytoskeletal system of the cell. We have tested the association between IF bundles and malignancy in lymphocytes in a series of 28 cases of cutaneous T cell lymphoma ie mycosis fungoides (MF), 26 cases of benign skin disorders, 17 controversial cases, and in eight cases of B cell lymphomas. An IF bundle was defined as at least five parallel IF in near longitudinal section on an electron-lucent background. Such bundles were found in 2 to 93 per cent of the cells in 27 of 28 MF cases, in 13 of 26 benign cases, and in 13 of 17 controversial cases. In contrast, only one of eight B cell lymphomas had a few cells with small IF bundles. In the benign cases, the IF bundles were small, whereas in MF the bundles were more prominent. The number of cells having such bundles as well as their prominence varied from case to case. IF bundles were observed both in very early and in late stages of MF. An increased prominence of IF bundles may serve as a secondary marker for distinguishing certain T from B cell lymphomas. (no Refs)

## 57. PRELIMINARY IMMUNOLOGICAL EVALUATION OF CARCINOMA OF THE BREAST AND THYROID GLAND.

**Abeatici S, Mussa A, Levis P, Sandrucci S, Storta P**
**Istituto di Clinica Chirurgica II, Universita di Torino, Turin, Italy**
**Minerva Med; 73(18):1145-1154 1982**

Immunological parameters were studied preoperatively and postoperatively in 15 women with malignant tumors (7 with thyroid lesions of the thyroid or of the breast). The total percentage of leukocytes and E rosettes showed a significant difference between the cancer patients and controls and was not affected by surgery. The percentage of B lymphocytes was higher in the cancer patients (2-70%, av 16.4%) than in the controls (4-20%, av 8.1%). The corresponding percentages after surgery were 12.8% and 6%, respectively. The cortisol levels were 100-400 nanog (ng)/ml for cancer patients and 100-250 ng/ml for controls. The mean values were 217.6 ng/ml for cancer patients vs 157.5 ng/ml for controls. The carcinoembryonic antigen (CEA) levels measured before surgery were significantly higher for the patients with thyroid carcinoma than for the patients with goiter. Significant reduction of CEA level was seen after surgery in the cancer patients compared with the preoperative levels. CEA levels were lower in the patients with breast cancer than in those with thyroid carcinoma, and did not differ to much from those measured in the patients with benign breast lesions. CEA levels of the breast cancer patients decreased to 2-3 ng/ml after a slight transient rise shortly after surgery. The IgA, IgG and IgM levels in the patients with thyroid carcinoma were higher than in the patients with

benign thyroid lesions. Surgery caused no significant changes in the immunoglobulin levels. (22 Refs) (In ITA)

## 58. IMMUNE STATUS OF UNTREATED PATIENTS WITH HODGKIN'S DISEASE AND PROGNOSIS.

**Bjorkholm M, Wedelin C, Holm G, Ogenstad S, Johansson B, Mellstedt H**

**Dept. Medicine, Div. Hematology, Danderyd Hosp., S-182 38 Danderyd, Sweden**

**Cancer Treat Rep; 66(4):701-709 1982**

In this study of 127 previously untreated adult patients with Hodgkin's disease and 167 age- and sex-matched controls, highly purified blood lymphocytes were studied for E+ receptors; their spontaneous DNA synthesis and that induced by concanavalin A, pokeweed mitogen, or purified protein derivative of tuberculin were measured as incorporation of 14C-thymidine. T-cell counts and the response to mitogens and antigen were significantly decreased in the patients, while the spontaneous lymphocyte activity was increased. Forty-nine patients had died after a mean observation time of 6 yr. In these patients, there had been an increase in spontaneous DNA synthesis and a decrease in that induced by mitogens and antigen. These differences also remained significant when patients who died were compared with surviving patients in Stages I-II. The 5-yr survival rate of 'bad immunology' patients was 30% as compared to 80% for the remainder. We suggest that these lymphocyte tests should be considered in an 'immunologic staging system,' which may give guidance in the future management of patients with Hodgkin's disease. (Author abstract) (25 Refs)

## 59. IMMUNOHISTOCHEMICAL ANALYSIS OF THE DISTRIBUTION OF LYMPHOCYTE SUBPOPULATIONS IN HODGKIN'S DISEASE.

**Borowitz MJ, Croker BP, Metzgar RS**
**Dept. Pathology, Duke Univ. Medical Center, Box 3712, Durham, NC, 27710**

**Cancer Treat Rep; 66(4):667-674 1982**

We studied the histologic distribution of lymphocyte subpopulations in Hodgkin's disease. Involved tissues from 15 patients were stained by an indirect immunoperoxidase procedure for a variety of lymphocyte surface antigens using monoclonal antibodies. In most cases, there were more T cells than B cells, and Reed-Sternberg cells were found in T-cell-rich areas. Except in lymphocyte-depleted Hodgkin's disease, helper-T antigen-positive (TH) cells greatly outnumbered cytotoxic-suppressor antigen-positive cells. Moreover, TH cells showed a preferential association with Reed-Sternberg cells. Lymphocytes surrounding Reed-Sternberg cells often expressed the transferrin receptor, a marker of cell activation. Our results do not support the hypothesis that the lymphocytes in Hodgkin's disease represent a cytotoxic T-cell response to neoplastic cells, except perhaps in the lymphocyte-depleted subtype. (Author abstract) (24 Refs)

## 60. A MEGAKARYOCYTIC THROMBOCYTOPENIA ASSOCIATED WITH AN EXCESS OF LEU 2A+ SUPPRESSOR CELLS.

**Worman CP, Mills KH, Linch DC, Beverley PC, Goldstone AH, Cawley JC**
**(c/o Cawley) Dept. Haematology, Univ. Coll. Hosp., Grafton Way, London WC1, England**

**Scand J Haematol; 28(3):215-219 1982**

Eight patients with acute myeloid leukemia (AML), either at presentation or in remission, had normal T-cell subsets as defined by Fc receptors and monoclonal antisera. In contrast, a persistent excess of T lymphocytes staining with Leu 2a (defining suppressor cells) was noted in a case of AML in which persistent amegakaryocytic thrombocytopenia occurred after other hemopoietic lines had recovered from ablative chemotherapy. It is suggested that the 2a+ cells were involved in the suppression of megakaryocytopoiesis, and the phenotype of the lymphoid cells is compared and contrasted with previously described cases of other cytopenias associated with an excess of suppressor cells. (Author abstract) (13 Refs)

# AUTHOR INDEX WITH CITATION NUMBERS


Abeatici S. 57
Aerts C. 35
Andersson LC. 12
Aoki T. 45
Arnold B. 53
Ash RC. 24
Baldwin RW. 50
Bamberger EG. 34
Basciano LK. 16
Basham TY. 41
Beauregard JC. 51
Bernard A. 17
Bertoglio J. 27
Beverley PC. 30
Beverley PC. 60
Biserte G. 35
Bjorkholm M. 58
Blanquet PR. 35
Bloch A. 31
Bluestone JA. 19
Boccadoro M. 6
Borowitz MJ. 59
Borowitz MJ. 9
Boumsell L. 17
Bourgeade MF. 41
Bressler J. 32
Brynes RK. 2
Burrichter H. 8
Carlson GP. 10
Cavallo G. 53
Cawley JC. 30
Cawley JC. 60
Chan WC. 2
Chang KS. 45
Check IJ. 2
Cheever MA. 47
Chiao JW. 32
Civin C. 31
Clarkson B. 32
Collins HA. 51
Creasey AA. 41
Crocker BP. 9
Croker BP. 59
Cupissol D. 48
Cuttito M. 43
D'Eustachio P. 49
Daynes RA. 37
Diehl V. 8
Dillman RO. 51
Dorsey JK. 5
Ezdinli EZ. 3
Favier F. 48
Fefer A. 47
Feldman BF. 10
Filatova NA. 46
Fleit HB. 15
Fonatsch C. 8
Gahmberg CG. 12
Gavarotti P. 6
Geisler C. 55
Gelfand EW. 33
Gelin C. 17
Gerdes J. 18
Gerdes J. 8
Giblett ER. 13
Goldstone AH. 60
Golish J. 11
Goiub SH. 42
Gomard E. 45
Gomard E. 54
Gordon D. 2
Gorlanov IA. 46
Gosse C. 17
Greenberg PD. 47
Habu S. 22
Hansen JA. 13
Hansen MM. 55
Hashimoto Y. 45
Hayashi H. 36
Heffner LT. 2
Heintz F. 8
Heit W. 8
Henney CS. 28
Henschel A. 55
Herberman RB. 45
Hindo J. 3
Hirashima M. 36
Hirohashi S. 52
Hirostu Y. 36
Hirshaut Y. 32
Holm G. 58
Holm G. 7
Hou-Jensen K. 55
Hyman R. 25
Ichiki AT. 34
Ino Y. 52
Isersky C. 16
Jansen J. 24
Johansson B. 58
Kaplan JH. 40
Kasai M. 22
Kersey JH. 24
Kirchner HH. 8
Knode MC. 19
Konda S. 1
Kondratieva NA. 39
Korotky VV. 39
Kotsay BR. 39
Landolfo S. 53
Lattime EC. 43
LeBien TW. 24
Lee LS. 40
Leporrier M. 4
Letarte M. 26
Letarte M. 33
Levis P. 57
Levy JP. 45
Levy JP. 54
Linch DC. 60
Lockwood SH. 40
Loginsky VE. 39
Lorimer G. 26
Lozzio BB. 34
Lozzio CB. 34
MacLachlan NJ. 10
Madewell BR. 10
Martin PJ. 13
Massain M. 6
Mazurok AA. 39
McNutt NS. 56
Meghji G. 26
Mel'nikov RA. 46
Mellstedt H. 58
Mellstedt H. 7
Mendelsohn J. 38
Merigan TC. 41
Metzgar RS. 59
Metzger JJ. 19
Mills KH. 60
Minowada J. 31
Morgan N. 29
Mussa A. 57
Negoro S. 23
Oettgen HF. 32
Ogenstad S. 58
Okamura J. 33
Okumura K. 22
Ozato K. 19
Paietta E. 20
Pecoraro GA. 43
Peest D. 7
Penick GD. 5
Petras R. 11
Pettersson D. 7
Pham D. 17
Pileri A. 6
Pinatel C. 27
Pinsky C. 32
Plesner T. 55
Ralfkiaer E. 55
Raynal B. 17
Reinisch CL. 29
Rey A. 48
Riethmuller G. 21
Roussel P. 35
Royston I. 51
Ruddle NH. 49
Sachs DH. 19
Sandrucci S. 57
Sarzotti M. 53
Savage R. 11
Schaadt M. 8
Scharfman A. 35
Schwarzmeier JD. 20
Sebek B. 11
Seon BK. 23
Serrou B. 48
Sharma BS. 44
Shawler DL. 51
Sherris D. 37
Sheveleva VS. 46
Shimosato Y. 52
Shishido H. 14
Simonov NN. 46
Sinclair TF. 3
Sing AP. 29
Siraganian RP. 16
Sobol RE. 51

Spangrude GJ..... 37
Stallings V..... 25
Stein H..... 18
Stein H..... 8
Storta P..... 57
Stutman O..... 43
Sueno K..... 8
Sugimoto T..... 31
Taetle R..... 38
Takeda K..... 31
Takiguchi T..... 1
Tatsumi E..... 31
To D..... 38
Trotter J..... 25
Trowbrdige I..... 25
Tubbs R..... 11
Uchanska-Ziegle..... 8
Unkeless JC..... 15
Urdal DL..... 28
Vorobel AV..... 39
Vygovskaya YI..... 39
Wedelin C..... 58
Weick J..... 11
Weiss R..... 11
Whitsett C..... 2
Wibier-Franqui..... 45
Worman CP..... 30
Worman CP..... 60
Wormsley SB..... 51
Wright SD..... 15
Wybier-Franqui..... 54
Zanjani ED..... 24
Ziegler A..... 8
Zuniga MC..... 49

# Keep Up with the Cancer Literature

## Each Month
## You Can Receive Abstracts
## Covering Your Specialty Area

- This convenient service — called Auto SDI* — is as near as your nearest biomedical library. Discuss your research interests with the librarian who will design an appropriate search strategy.
- Abstracts of the latest published literature are searched automatically each month and those related to your interests are delivered to you on a regular basis.
- The abstracts you receive are selected from more than 4,000 monthly entries made into CANCERLIT — the extensive cancer literature data base of the National Cancer Institute.

## Talk With Your Librarian
## About the Auto SDI Service TODAY.

*Auto SDI stands for Automatic Selective Dissemination of Information. It is a service provided to you, at minimal cost, by the International Cancer Research Data Bank (ICRDB) — a part of the National Cancer Institute.

☆U.S. GOVERNMENT PRINTING OFFICE: 1982-381-847:202

# Compilation of Experimental Cancer Therapy Protocol Summaries

April 1982
Sixth Edition

COMPLIMENTARY COPIES NOW AVAILABLE

## CONTENT

This document contains summaries of over 1200 open experimental clinical cancer therapy protocols from countries around the world.

Open protocols are arranged in sections according to the specific type of cancer.

Protocols closed in 1981 are listed by title, number, and investigator in a separate section.

## INDEXES

Tumor index
Agent/Modality index
Protocol identification number index

---

Request for 1982 COMPILATION.
(Print Clearly for use as mailing label)

Name: _____

Address: _____

_____

City/State/Zip: _____

Country: _____

Mail to:
Compilation Request
ICRDB Program
National Cancer Institute
Westwood Building Room 10A18
Bethesda, Maryland 20205

**U.S. DEPARTMENT OF COMMERCE**
**National Technical Information Service**
5285 Port Royal Road
Springfield, Va. 22161

OFFICIAL BUSINESS

Penalty for Private Use, $300

**PRINTED MATTER**

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF COMMERCE
COM-211

THIRD CLASS
BULK RATE

U.S.MAIL

CB-17

**CANCERGRAMS are distributed for the International Cancer Research Data Bank (ICRDB) by the National Technical Information Service (NTIS). CANCERGRAMS are available from NTIS on a standing order basis at $2 each for North American Continent addressees and $3 each for other addressees. An NTIS deposit account is required. For a list of subject categories or other information, please write to:**

**Subscription Section**
**National Technical Information Service**
**5285 Port Royal Road**
**Springfield, VA 22161**

**NOTICE OF MAILING CHANGE**

☐ Check here if you wish to discontinue receiving this publication.

☐ Check here if your address has changed and you wish to continue receiving this publication. (Be sure to furnish your complete address including zip code.)

Tear off cover with address label still affixed and send to:

Computer Support Center
ICRDB Program
IIT Research Institute
10 West 35th Street
Chicago IL. 60616

CB17/82/11

NCI/ICRDB/CB17 82/11

P982-931811

# ICRDB CANCERGRAM

# IMMUNOBIOLOGY AND CANCER

## Identification and Characterization of Immune Cells

SERIES CB17 No. 82/11 NOVEMBER, 1982

This Cancergram is a service of the INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM of the U.S. National Cancer Institute. Every few weeks, an updated Cancergram containing abstracts of selected cancer-related articles recently published in more than 3000 journals, and dealing with the topic indicated by the above title, is sent to researchers working in this area. These researchers are identified on the basis of the description of their current research project that has been submitted to the ICRDB Program, directly or via granting agencies.

This Cancergram is prepared by the Cancer Information Dissemination and Analysis Center (CIDAC) for Virology, Immunology, and Biology. ***If this Cancergram is useful and valuable, please send your comments to the CIDAC address below, since future editions depend on user satisfaction and user needs:***

CIDAC FOR VIROLOGY, IMMUNOLOGY, AND BIOLOGY
SCIENCE INFORMATION SERVICES
FRANKLIN INSTITUTE RESEARCH LABORATORIES
20TH AND RACE STREETS
PHILADELPHIA, PA 19103

NEWARK PUBLIC LIBRARY
NOV 18
U. S. GOVT. PUBS.
DEPOSITORY 376

*In this issue:*


- CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS..... 1-15
- DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS..... 16-21
- LYMPHOCYTE AND DIFFERENTIATION ANTIGENS..... 22-40
- CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION..... 41-44
- EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS..... 45-48
- OTHER RELATED STUDIES..... 49-59


## CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS

### 1. E RECEPTOR EXPRESSION OF T LYMPHOCYTES IN T LYMPHOPROLIFERATIVE DISEASES.

**Jonsson V, Andersen BL, Brandrup F, Christensen BE, Rothenborg HW, Thomsen K**
**Medical Dept. C., Hematology Lab., Gentofte Univ. Hosp., 2900 Hellerup/Copenhagen, Denmark**
**Scand J Haematol; 28(4):329-334 1982**

The lymphoid component of skin infiltrates from six cases of mycosis fungoides and two cases of T cell chronic lymphatic leukemia consisted almost exclusively of T lymphocytes with abnormally high E receptor expression. Such T cells were also found to dominate the skin infiltrates from 10 patients with severe atopic dermatitis. Blood T lymphocyte counts from all types of patients were within the normal range, but even the blood T lymphocytes of the patients had a strong E receptor expression. The bone marrow in atopic dermatitis and in mycosis fungoides showed normal T cell counts with normal E receptor expression. Supported by basic lymphocyte-kinetic



HE 20.3173/2:

considerations it is likely that the skin in T lymphoproliferative diseases is characterized by an abnormal ability to home and/or to trap T lymphocytes with strong E receptor expression. (Author abstract) (22 Refs)

## 2. VIL-A1, A MONOCLONAL ANTIBODY REACTIVE WITH COMMON ACUTE LYMPHATIC LEUKEMIA CELLS.

Knapp W, Majdic O, Bettelheim P, Liszka K
Inst. Immunology, Borschkegasse 8A, A-1090 Vienna, Austria
Leuk Res; 6(2):137-147 1982

Generation and characterization of a monoclonal antibody (VIL-A1) raised against Reh cells which specifically reacts with the common acute lymphoblastic leukemia associated (CALL) antigen are described. Immunoelectrophoresis of VIL-A1 showed that the antibody is of the IgM kappa type. Several established human cell lines were tested for their reactivity with VIL-A1 and the reactivity patterns are presented. The reactivity of VIL-A1 with leukemic cells from 97 patients were tested by immunofluorescence. Positive reactions were observed in non-B, non-T acute lymphatic leukemias and in terminal deoxynucleotidyl transferase (TdT) positive chronic myeloid leukemia blast crisis. The reactivity pattern of VIL-A1 and J5 was absolutely identical. VIL-A1 reacted with a membrane component of Reh-6 cells with a mol wt of approx 95,000 daltons. No VIL-A1 reactive component was detected in Raji cells. Not all VIL-A1 antigen bound to lecithin and the binding capacity was heterogenous. Unlabeled VIL-A1 antibody very efficiently blocked the binding of peroxidase-labeled VIL-A1 antibody to a CALL membrane preparation coated on polystyrene tubes. Preincubation with J5 antibody under capping conditions restricted the binding of VIL-A1 antibody, although incubated under non-capping conditions, to one pole of the cell and preincubation with VIL-A1 antibody under capping conditions restricted the binding of J5 antibody to one pole of the cell. Preincubation with negative control antibody had no such effect and left the normal diffuse and ring-staining pattern of both antibodies unchanged. Results showed that the VIL-A1 monoclonal antibody raised against Reh cells reacts with CALL cells but not with normal or malignant B or T lymphocytes. (34 Refs)

## 3. ROSETTE FORMATION BETWEEN CHRONIC T-LYMPHOCYTIC LEUKEMIA CELLS AND MACROPHAGES: A FACSIMILE OF NORMAL T-LYMPHOCYTE-MACROPHAGE COOPERATION.

Jennette JC, Benson JD, Wilkman AS
Dept. Pathology, Sch. Medicine, Univ. North Carolina, Chapel Hill, NC, 27514
Am J Hematol; 12(3):301-304 1982

Neoplastic T lymphocytes from a patient with chronic T-lymphocytic leukemia formed rosettes with macrophages. It is proposed that this phenomenon represents retention by these abnormal cells of the normal ability of T lymphocytes to associate physically with macrophages. Recognition of rosettes between benign macrophages and leukemia or lymphoma-derived lymphocytes may indicate T-cell lineage of the neoplastic lymphoproliferation. (Author abstract) (9 Refs)

## 4. IMMUNOLOGIC DIAGNOSIS OF LYMPHOID LEUKEMIAS: PRELIMINARY REPORT (MEETING ABSTRACT).

Cruz C, Carnot J, Svarch E, Santos MN, Ballester JM, Hernandez P
No affiliation given
Sangre (Barc); 26(5A):662 1981

At the present time it appears that from a cellular standpoint chronic lymphatic leukemia usually consists of neoplastic exacerbation of a lymphocyte clone of B origin. T variants occur much less frequently, and on rare occasions lymphocytes bearing mixed T and B receptors are found. Something similar occurs in lymphoblastic leukemia with the difference that in this disease the majority of cases have no surface markers (null type). It is argued that they have lost them or have not expressed them in view of the degree of immaturity of the cells involved in this process. Lymphoid leukemias are currently being diagnosed immunologically in a great number of countries. This approach holds promise since it makes it possible to classify these leukemias into different subgroups yielding diagnostic, prognostic, and, at times, therapeutic advantages. In the present paper we perform the broadest battery of tests possible which will detect lymphocyte markers thus enabling a more precise classification of lymphoid leukemias from an immunologic standpoint. The tests performed and the av values obtained in healthy subjects are listed below. The number of subjects in each test is given in parentheses. Of 9 children with lymphoblastic leukemia, 4 were identified as T variant because of spontaneous rosetting (SR) values of 40% or more; 3 were classified as possible T variants with SR values between 20 and 40%. One patient was classified as B variant because of surface immunoglobulins (SIg) of 50%. The 2 remaining were considered null variants since none of the markers studied were elevated. Out of a group of 9 adults with chronic lymphoid leukemia, 1 was classified as T variant because of a SR value of 70%; 5 were regarded as B variant on account of SIg greater than 50% and 2 of them had mouse rosettes (MR) greater than 40%. The 3 remaining were considered null variants because they showed no significant increase in any of the markers studied. (no Refs) (In SPA)

## 5. OBSERVATION OF SURFACE MARKERS ON LEUKEMIC CELLS IN THREE CASES OF CHRONIC LYMPHATIC LEUKEMIA.

Park K, Kamitani T, Tatsumi Y, Im TS, Tatsumi N, Kimura Y, Mahda H, Okuda K, Yamamoto S
Dept. Clinical and Laboratory Medicine, Osaka City Univ., Osaka, Japan
Rinsho Ketsueki; 23(1):91-99 1982

Surface markers on leukemic cells were examined in three cases of chronic lymphatic leukemia (CLL). The chronic lymphatic leukemia was diagnosed by means of dry bone marrow taps in three men (57, 60, and 76 yr old, respectively). All three cases had marked proliferation of WBC, a large proportion of which were mature-type lymphocytes and a small percentage of which were prolymphocytes or lymphoblasts. Two of the cases had low phytohemagglutinin-induced blastogenic response, anemia, and thrombocytopenia. According to investigation using antisera IgF(ab2) fragments, two of the cases were thought to be classifiable as surface immunoglobulin negative non-T CLL. The other case was thought to be immunoglobulin class IgD or IgD + IgG type immunoglobulin positive B-CLL. C3b and C3d receptors were observed on the cells of the non-T CLL cases, but the C3b positive cells were more abundant. Cells collected from the patients' lymph nodes showed that the C3d receptors were more abundant than the C3b re-

ceptors. Thus, observations of both surface markers on peripheral leukemic cells and lymph node cells were thought to be important. (21 Refs) (In JPN)

## 6. FUNCTIONAL PROPERTIES OF T CELLS IN PATIENTS WITH CHRONIC TGAMMA LYMPHOCYTOSIS AND CHRONIC T CELL NEOPLASIA.

**Rumke HC, Miedema F, Ten Berge IJ, Terpstra F, Van der Reijden HJ, Van de Griend RJ, De Bruin HG, Von dem Borne AE, Smit JW, Zeijlemaker WP, Melief CJ**
**(c/o Melief) Dept. Tumor Immunology, Central Lab., The Netherlands Red Cross Blood Transfusion Service, P.O. Box 9190, 1006 AD Amsterdam, The Netherlands**
**J Immunol; 129(1):419-426 1982**

The expanded T cell populations of 10 patients with either T gamma lymphocytosis (5 patients) or proven chronic T cell malignancy (5 patients) were analyzed with respect to functional activity in vitro, including proliferative responses to mitogens, cytotoxic activity (killer [K] and natural killer [NK] cell activity), and regulatory activity on pokeweed mitogen-(PWM) induced immunoglobulin (Ig) synthesis (help and suppression) in comparison with marker phenotypes. In each of the five patients with Tgamma lymphocytosis, only one out of three functionally distinct cell types was found: Tgamma-K cells, Tgamma-S cells, or Tgamma-NK/K cells, which mediated K-cell activity, suppressive activity and both NK and K cell activity, respectively. An expanded Tgamma-K cell population was demonstrated in three patients with neutropenia with or without recurrent infections. Tgamma-S cells were found in a patient with severe hypogammaglobulinemia, and Tgamma-NK/K cells in one patient with asymptomatic lymphocytosis. Tgamma-K and Tgamma-S cells had a similar surface-marker profile (E+ or E-, Fcgamma+, OKT1(-)3+4(-)8+11-M1(-)), whereas that of Tgamma-NK/K cells was different (E+, Fcgamma+, OKT1(-)3(-)4(-)8-11+M1+). Longitudinal studies of three untreated patients with Tgamma-K lymphocytosis showed that the abnormalities were persistent but not progressive. In contrast, five patients with chronic T cell malignancy (2 with T-CLL, 2 with cutaneous T cell lymphoma [CTCL], and 1 with T-PLL) all had progressive disease. The neoplastic cells in these cases were E+, Fc gamma-OKT1+4+6(-) with variable expression of the OKT3 and OKT8 markers. The only functional activity observed in these cells was suppressive activity by OKT3(-)4+8(-) cells from a patient with CTCL. (Author abstract) (50 Refs)

## 7. CHRONIC LEUKEMIA WITH A HYBRID SURFACE PHENOTYPE (T LYMPHOCYTIC/MYELOMONOCYTIC): LEUKEMIC CELLS DISPLAYING NATURAL KILLER ACTIVITY AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY.

**Schlimok G, Thiel F, Rieber EP, Huhn D, Feucht H, Lohmeyer J, Riethmuller G**
**Medical Clinic II, Langemarckstr. 11, 8900 Augsburg, W. Germany**
**Blood; 59(6):1157-1162 1982**

A patient with chronic leukemia exhibited uncommon clinical features, such as hypergammaglobulinemia and activation of intravascular coagulation after low-dose irradiation of the enlarged spleen. By light and electron microscopy, the leukemic cells resembled large granular lymphocytes. The following markers were simultaneously expressed on their surface: receptors for sheep erythrocytes and the Fc part of IgG; common T-cell antigens as revealed by a heteroantiserum (HuTLA) and monoclonal antibodies (OKT3, T411); antigens shared by cytotoxic/suppressor T cells (OKT8, T811) as well as myelomonocytic antigens defined by the OKM1 and M522 monoclonal antibodies. The leukemic cells showed both spontaneous (NK) and antibody-dependent (ADCC) cytotoxicity, but they did not suppress B-cell differentiation in vitro. (Author abstract) (40 Refs)

## 8. SURFACE IMMUNOGLOBULINS ON HAIRY CELLS OF 55 PATIENTS WITH HAIRY CELL LEUKEMIA.

**Golomb HM, Davis S, Wilson C, Vardiman J**
**Box 420, 950 East 59th St., Chicago, IL, 60637**
**Am J Hematol; 12(4):397-401 1982**

Surface immunoglobulins (SIg) were determined on peripheral blood samples from 55 patients with hairy cell leukemia (HCL) and on hairy cells from spleen preparations of 14 of these 55 patients. The patterns of SIg for HCL was compared to the patterns on peripheral blood leukemic cells from 39 patients with chronic lymphocytic leukemia (CLL) and 15 patients with poorly differentiated lymphocytic (PDL) lymphoma. Of the 55 HCL patients, 42 could be scored for individual heavy and light chains; 16 had only IgG, 14 had two or three heavy chains, 7 had only IgD, and 5 cases had no SIg and were E-rosette negative. This pattern was different from the B-cell pattern in CLL and PDL where there were few cases of IgG alone (5%) and many cases of IgM alone (50%). Surface marker profile did not correlate with survival in any of the sub-groups tested. HCL appears to be a B-cell lymphoproliferative disease in greater than 90% of cases; many combinations of heavy chains with only a single light chain can be demonstrated. (Author abstract) (14 Refs)

## 9. A MONOCLONAL ANTIBODY WITH ANTI-BURKITT LYMPHOMA SPECIFICITY. I. ANALYSIS OF HUMAN HAEMATOPOIETIC AND LYMPHOID CELL LINES.

**Wiels J, Lenoir GM, Fellous M, Lipinski M, Salomon JC, Tetaud C, Tursz T**
**Laboratoire d'Immunologie Clinique, Institut G. Roussy, Rue C. Desmoulins, 94800 Villejuif, France**
**Int J Cancer; 29(6):653-658 1982**

There is a hybridoma-produced monoclonal rat IgM (38-13) which appears to define a Burkitt's lymphoma-associated antigen (BLA). In this paper, we describe the reactivity of 38-13 with a panel of human hematopoietic and lymphoid cell lines. In indirect immunofluorescence (IF) assays, 15 of 26 Burkitt's lymphoma (BL) lines studied were clearly stained with 38-13 (from 13 to 100% positive cells) by microscope, with varying numbers of heavily labeled cells. In these positive cell lines, fluorescence-activated cell-sorter (FACS) analysis demonstrated that BLA was actually present on all the cells. Positive BL included Epstein-Barr virus (EBV) genome-carrying lines and EBV-negative ones; thus, BLA is not related to the presence of EBV. Most of the 15 BL cells that reacted with 38-13 contained a typical t(8;14) translocation, but had variant translocations such as t(2;8) and t(8;22). The cells were derived from BL patients of different geographical origins and clinical features. Four BL lines were poorly stained and seven were negative with 38-13 in IF assays. The 32 EBV-positive lymphoblastoid cell-lines (LCL) studied were negative. In three line pairs, consisting of a tumor line and an LCL from the same patient, only the BL line was demonstrated to react with 38-13. A series of non-BL cells, including hematopoietic, lymphoid and solid tumor lines, all failed to react with 38-13. Various attempts to modulate the expression of BLA on BL cells were unsuccessful. However, it cannot be ruled out that BLA is actually a transient B-cell differentiation marker. (Author abstract) (18 Refs)

## 10. IMMUNITY AND HYPERSENSITIVITY IN HODGKIN'S DISEASE.

Leoni P, Marchegiani G, Montillo M, Centurioni R, Montroni M, Danieli G

Istituto di Patologia Speciale Medica e Metodologica Clinica, Universita di Ancona, Ancona, Italy

Minerva Med; 73(20):1361-1369 1982

Some immunological parameters (absolute count and percentage of lymphocytes, E rosettes and lymphocytes with S immunoglobulin (S-Ig)) were studied in 47 patients with Hodgkin's disease (HD). The percentages of lymphocytes were found to be 33% in Stage I, 26% in II, 21% in III and 20.7% in IV; 46% in lymphocyte predominant (LP) type, 22.3% in nodular sclerotic (NS) Type, 27.6% in mixed cellular (MC) Type and 24.6% in lymphocyte depleted (LD) Type. The percentages of E rosettes were 58% in Stage I, 50.8% II, 52% in III and 50% in IV; 35% in LP Type, 53.1% in NS Type, 46.6% in MC Type and 45.5% in LD Type. The percentages of lymphocytes with S-Ig were 17% in Stage I, 32% in II, 35.5% in III and 24.3% in IV; 22.9% in LP Type, 31.7% in NS Type, 30.5% in MC Type and 38% in LD Type. Functional and anatomic depression of the T-cell system is prevalent or exclusive in patients with Stages III and IV of HD of MC and LD Type. Studied on immunological changes and their causes in patients with HD are reviewed. (111 Refs) (In ITA)

## 11. THE CORRELATION OF ADENOSINE DEAMINASE AND PURINE NUCLEOSIDE PHOSPHORYLASE ACTIVITIES IN HUMAN LYMPHOCYTES SUBPOPULATIONS AND IN VARIOUS LYMPHOID MALIGNANCIES.

Demeocq F, Viallard JL, Boumsell L, Richard Y, Chassagne J, Plagne R, Lemerle J, Bernard A

Centre Jean Perrin, B. P. 392, 63011 Clermont-Ferrand Cedex, France

Leuk Res; 6(2):211-220 1982

Activities of adenosine deaminase (ADA) and purine nucleotide phosphorylase (PNP) were measured in normal human T cells and in the tumor cell populations from 62 children and 27 adults with lymphoid malignancies. Thymocytes had high ADA activity and low PNP activity, whereas T-peripheral blood lymphocytes (PBL) had low ADA activity and high PNP activity. Malignant B-cell populations had low values of ADA activities and intermediate values of PNP activities similar to E rosette formation negative PBL. Non-T, non-B acute lymphocytic leukemia (ALL) patients had cells with high values of ADA activities and moderate values of PNP activities. A linear correlation between ADA and PNP activities was observed in cells from non-T, non-B ALL, whereas such a correlation did not appear in cells from T-ALL or T-lymphoblastic lymphomas. HLA-DR negative common ALL cell populations had high values of ADA as compared to HLA-DR positive common ALL cell populations. In contrast with HLA-DR, presence or absence of common ALL antigen, as defined by Mo.Ab J5, did not appear to correlate with the level of the enzyme activities. Particularly no clear distinction between the subgroup of malignancies that could be related to corticothymocytes and the subgroup related to medullary thymocyte in terms of both ADA and PNP activities could be disclosed, and large ranges of values were observed in both subgroups. No correlation appeared to occur in the group of T-cell lymphoid malignancies, whereas a correlation existed in cells from children with non-T, non-B ALL. (37 Refs)

## 12. ADENOSINE DEAMINASE AND PURINE NUCLEOSIDE PHOSPHORYLASE ACTIVITIES OF VARIOUS CULTURED CELL LINES DERIVED FROM HUMAN HEMATOLOGIC MALIGNANCIES.

Hirose M, Minato K, Shimoyama M

Dept. Clinical Lab. and Internal Medicine, Natl. Cancer Center Hosp., Tokyo, Japan

Nippon Ketsueki Gakkai Zasshi; 45(3):555-561 1982

Activities of adenosine deaminase (ADA) and purine nucleoside phosphorylase (PNP) were measured in cultures of human hematopoietic malignant tumor cells, and the activities of the various cell lines were compared. The comparison of the cell lines was based on the lineage of the cell lines and groupings of the cell lines with respect to cell surface markers. The cell lines were derived from patients with acute lymphocytic leukemia, blastic crisis of chronic myelogenous leukemia, adult T-cell leukemia, Burkitt's lymphoma, acute promyelocytic leukemia, acute monocytic leukemia, acute myeloid leukemia, and chronic myelomonocytic leukemia. ADA activity was high in the T-cell type cultured strains of malignant tumor cells, especially for those T-cell lines that had the same cell surface markers as common thymocytes (T1 cells). No difference was observed between ADA activities of the five nonT nonB-cell lines, five B-cell lines, and five normal B-cell lines. ADA activity was lowest in the myeloid cell lines. No significant differences were observed between the PNP activities of any of the cell lines. ADA activity may be useful for differentiation of T-cell lineage. (44 Refs) (In JPN)

## 13. IMMUNOPATHOLOGY OF B-CELL LYMPHOMAS INDUCED IN C57BL/6 MICE BY DUALTROPIC MURINE LEUKEMIA VIRUS (MULV).

Pattengale PK, Taylor CR, Twomey P, Hill S, Jonasson J, Beardsley T, Haas M

Dept. Pathology, Univ. Southern California Sch. Medicine, 2025 Zonal Ave., Los Angeles, CA, 90033

Am J Pathol; 107(3):362-377 1982

Combined clinicopathologic and immunomorphologic evidence is presented that would indicate that a murine leukemia virus (MuLV) with the dualtropic host range is capable of producing a clinically malignant lesion composed of immunoblasts and associated plasma cells in C57BL/6 mice. This process, morphologically diagnosed as an immunoblastic lymphoma of B cells using standard histopathologic criteria, was found to be distinctly polyclonal with regard to immunoglobulin (Ig) isotype when analyzed for both surface and cytoplasmic Ig. Further studies demonstrated that this clinicopathologically malignant, dualtropic MuLV-induced, polyclonal immunoblastic lymphoma of B cells in C57BL/6 mice was normal diploid and unable to be successfully transplanted to nonimmunosuppressed syngeneic recipients. Although all serum heavy and light chain components were found to be progressively elevated as the tumor load increased, the polyclonal increase in serum immunoglobulins was most pronounced for mu heavy and kappa light chains (ie, mu greater than gamma2A greater than alpha greater than gamma 2B greater than gamma1; kappa greater than lambda). The dissociation of clinicopathologic and biologic criteria for malignancy in the presently described dualtropic (RadLV) MuLV-induced B-cell lesion is sharply contrasted with the thymotropic (RadLV), MuLV-induced T-cell lymphoblastic lymphoma in C57BL/6 mice. This process is also a clinicopathologically malignant lesion but, when one uses biologic criteria, is found to be distinctly monoclonal, aneuploid, and easily transplanted to nonimmunosuppressed syngeneic recipients. The close clinicopathologic and biologic similarities of

the dualtropic MuLV-induced animal model to corresponding human B-cell lymphoproliferative diseases are stressed. (Author abstract) (46 Refs)

### 14. MALIGNANT HISTIOCYTOSIS OF THE INTESTINE: REPORT OF THREE CASES WITH IMMUNOLOGICAL AND CYTOCHEMICAL ANALYSIS.

Isaacson P, Jones DB, Sworn MJ, Wright DH
Dept. Pathology, Southamptom Univ. Medical Sch., Level E, South Laboratory Block, Southampton SO9 4XY, England
J Clin Pathol; 35(5):510-516 1982

Tumor cells from three cases of malignant histiocytosis of the intestine (MHI) have been studied immunologically and cytochemically. The cells did not form E rosettes and showed weak Fcγ surface receptors. They contained non-specific esterase and acid phosphatase in diffuse granular distribution. In one case tumor cells showed no staining by an immunoperoxidase technique with two monoclonal anti-T cell antibodies but positive staining with a monoclonal anti-Ia-like antibody. The malignant cells from all three cases could be shown to contain alpha-1-antitrypsin. These are the first cases of MHI to have been studied in this way and the results confirm the true histiocytic - that is, monocyte/macrophage, derivation of the tumor cells in this disease. (Author abstract) (20 Refs)

### 15. CHARACTERIZATION OF PERIPHERAL LYMPHOID CELLS (DOWNEY CELLS) DURING INFECTIOUS MONONUCLEOSIS (IM), USING MONOCLONAL ANTIBODIES (MEETING ABSTRACT).

Fjelde A, Ozer H, Xellam J, Bennett P
Roswell Park Memorial Institute, Buffalo, NY, 14263
In Vitro; 18(3,part2):309 1982

The present study is part of a project concerning the relationship of IM and human lymphoma-leukemia, in which we have reported the presence of Paul-Bunnell (PB) antigen, the antibody which is present in high titer and diagnostic for IM. The present study is an investigation of the nature of the peripheral blood cell population in terms of surface antigens, using monoclonal antibodies and the cell sorter. A preliminary study using other methods showed an absolute increase in T lymphocytes. During early (1st week) IM, we found that a high percentage of responders to monoclonal antibodies repesented T cells, suppressor-cytotoxic (SC) cells and E rosette responding cells. At 1 month peripheral T cells (OKT-3) remained high, but all other values returned to normal or below. Response to OKT-4 antibodies representing helper-inducer T cells (H), was low at both periods. Values for OKT-6, 8, 11a OKIa and OKM1 were above normal at 1 week, but returned to normal at 1 month. The H/SC ratio was less than 1 at both periods, demonstrating an inversion of the normal values. Induction of IM by EM virus infection of B lymphocytes causes T cell reactive Downey cell proliferation, apparently representing a control system. (no Refs)

## DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS

### 16. MOUSE ROSETTE (M ROSETTE) IN THE DIFFERENTIAL DIAGNOSIS OF LYMPHOPROLIFERATIVE DISORDERS.

Gabrielli A, Leoni P, Marchegiani G, Montillo M, Centurioni R, Montroni M, Danieli G
Istituto di Patologia Speciale Medica e Metodologia Clinica, Universita di Ancona, Ancona, Italy
Minerva Med; 73(20):1383-1390 1982

The capacity of a subpopulation of human B lymphocytes to form nonimmune rosettes with mouse red blood cells (M rosettes) was used for the differential diagnosis of B-cell lymphoproliferative diseases in 24 patients (12 men and 12 women, 51-77 yr old) with chronic lymphocytic leukemia (CLL), 7 with leukemic lymphoma (LL) and 3 with hairy-cell leukemia (HCL). Four of the 24 patients CLL were in Stage 0, 16 in Stages I-II and 4 in Stages III-IV. The percentages of M rosettes were distinctly increased in the patients with HCL and LL. The percentage of M rosettes remained extremely elevated at lymphocyte counts below 10,000/cubic mm. The absolute counts of lymphocytes carrying this membrane receptor was found to increase with increasing lymphocyte count, which is an expression of the neoplastic population, and with the advancement of the clinical stage according to Rai's classification. (11 Refs) (In ITA)

### 17. MOUSE RED CELL ROSETTE FORMATION AND THE COLCHICINE SENSITIVITY TEST: RELATIVE USEFULNESS IN THE DIFFERENTIAL DIAGNOSIS OF CHRONIC LYMPHOCYTIC LEUKAEMIA AND B LYMPHOCYTIC LYMPHOMA.

Sugden PJ, Lilleyman JS
(c/o Lilleyman) Dept. Haematology, Children's Hosp., Sheffield S10 2TH, England
J Clin Pathol; 35(4):376-379 1982

Mouse erythrocyte (M) rosette formation and colchicine sensitivity were compared for their ability to differentiate chronic lymphocytic leukemia (CLL) from B cell non-Hodgkin's lymphoma (NHL) with overspill. Twenty-two cases of CLL and 8 of NHL were studied along with 31 normal adults. Results from the patients in both tests differed significantly from the controls but colchicine sensitivity failed to differentiate them further. M rosettes, on the other hand, while increased in some patients with NHL were, without overlap, much more numerous in those with CLL, and clearly distinguished the two conditions. A significant autolymphocytotoxic effect of plasma from both study groups was also noted which was not found in the controls. (Author abstract) (12 Refs)

### 18. THE ULTRASTRUCTURAL LOCALIZATION OF IMMUNOGLOBULINS IN HUMAN B CELLS OF IMMUNOPROLIFERATIVE DISEASES.

Gourdin MF, Farcet JP, Reyes F
(c/o Reyes) INSERM U.91, Hopital Henri Mondor, 94010 Creteil, France
Blood; 59(6):1132-1140 1982

The cellular distribution of immunoglobulins in human malignant and normal B cells was investigated by immunoelectron microscopy by direct incubation of fixed cells with peroxidase-coupled antibody. These conjugates penetrated into the cell,

resulting in the simultaneous detection of surface and cytoplasmic immunoglobulins. The latter were seen as specific intracisternal staining of the perinuclear space and endoplasmic reticulum and occasionally of the Golgi complex. Plasma cells were frequently characterized by a heterogeneity of reactivity of the endoplasmic reticulum. Minute amounts of cytoplasmic immunoglobulin were demonstrated in cells without developed secretory organelles, such as lymphoma cells and lymphocytes from chronic lymphocytic leukemia (CLL). The method allowed us to define several subsets of cells according to the expression of surface and cytoplasmic immunoglobulins and thus to determine the stage of maturation of cells involved in monoclonal proliferation. (Author abstract) (36 Refs)

### 19. FLUORESCEINATED LECTINS AS PROBE FOR CELL SURFACE CHANGES ASSOCIATED WITH LYMPHOCYTE TRANSFORMATION.

Strauchen JA
Palo Alto Veterans Admin. Medical Center, Palo Alto, CA, 94305
Am J Hematol; 12(3):227-232 1982

Lectins are plant-derived proteins with specific affinities for simple or complex sugars and are potentially useful tools for investigation of the carbohydrate structure of the cell surface. A panel of fluoresceinated lectins was used to study the cell surface changes associated with lymphocyte transformation. The major determinants detected on peripheral blood lymphocytes were alphaD-mannose,beta-D-galactose and N-acetyl-glucosamine. Phytohemagglutinin transformation was associated with increased binding of lectins specific for N-acetyl-galactosamine. MOLT-4, a T-lymphoblast cell line in continuous culture, was associated with increased binding of lectins specific for N-acetyl-galactosamine and L-fucose. Application of fluoresceinated lectins may be a useful tool in the classification of lymphoid cells. (Author abstract) (10 Refs)

### 20. LOSS OF SURFACE-BOUND ANTIBODY ACCOMPANYING THE ANTI-COMPLEMENTARY MODULATION OF LEUKEMIC B CELL IMMUNOGLOBULIN: CONTRASTING EFFECTS OF ANTIBODIES DIRECTED AGAINST IDIOTYPIC AND CONSTANT REGIONS.

Gordon J, Anderson VA, Stevenson GT
Dept. Tumor Biology, Karolinska Inst., Box 60400, S-104 01 Stockholm, Sweden
J Immunol; 128(6):2763-2769 1982

Guinea pig L2C leukemia lymphocytes display at their surfaces monoclonal IgM, which when complexed with antibody undergoes rapid redistribution and variable endocytosis. One consequence of this is that the cells can prove resistant to lysis by complement subsequently added to the system, a process termed here anti-complementary modulation. We studied quantitatively the extent of antibody loss accompanying the modulation by radioimmunolabeling the cell surfaces with 125I-Fab'-gamma fragments from an anti-antibody. Antibody directed against the constant region of the IgM light chain (anti-lambda) gave modulation effective against syngeneic (guinea pig strain 2) complement that closely paralleled the disappearance of anti-lambda from the cell surfaces. Antibody directed against the idiotypic region of the light chain (anti-Id) was as effective as anti-lambda in modulating against syngeneic complement. However, the bulk of the anti-Id was seen by radioimmunolabeling to persist on the surfaces of the resistant cells, even after prolonged exposure at 37 C, and was shown by immunofluorescence to be in a patched configuration. In contrast to the results with syngeneic complement, modulation effective against rabbit complement appeared to have an absolute requirement for clearing of the antibody: thus anti-lambda could modulate, anti-Id could not. The differences observed between anti-lambda and anti-Id could not be accounted for by differences in their isotypic (Ig subclass) composition nor by the numbers of antibody molecules bound. Studies with directly fluoresceinated and 125I-labeled and anti-lambda revealed endocytosis rather than shedding was the major route of antibody loss from the cell surfaces over the period of anti-complementary modulation. The findings are discussed in relation to mechanisms that enable leukemic B lymphocytes to escape destruction when confronted by antibody and complement. (Author abstract) (32 Refs)

### 21. IMMUNOGLOBULIN PRODUCTION AFTER MARROW TRANSPLANTATION. III. THE FUNCTIONAL HETEROGENEITY OF FC-IGG RECEPTOR POSITIVE AND NEGATIVE T CELL SUBPOPULATIONS.

Lum LG, Seigneuret MC, Orcutt-Thordarson N, Ostenson RC, Storb R
Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
Clin Exp Immunol; 48(3):675-684 1982

Ten patients with chronic graft-vs-host disease (GVHD) after HLA-identical marrow transplantation were studied between 372 and 1,649 days post-transplant for their T cell subset functions in pokeweed mitogen-stimulated immunoglobulin (Ig) synthesis. In vitro Ig synthesis was assessed using an indirect hemolytic plaque assay after 6 days of culture. T cells, TG+ cells (Fc-IgG receptor positive), TG- cells (Fc-IgG receptor negative), and B cell-enriched populations from the patients were co-cultured with normal T and/or B cells. Such cultures in patients with chronic GVHD showed deficient B cell activity (8 of 10); and deficient helper activity in T cells (6 of 10), TG+ cells (5 of 9), and TG- cells (3 of 9). Greater than 50% suppression of Ig synthesis was detected with T cells (4 of 10), TG+ cells (3 of 10), and TG- cells (3 of 10). This study provides evidence for variable regulatory function of Fc receptor T cell subsets in patients with chronic GVHD. The unexpected finding was that TG+ and TG- subpopulations can lack helper activity or actively suppress Ig synthesis. (Author abstract) (32 Refs)

## LYMPHOCYTE AND DIFFERENTIATION ANTIGENS

### 22. EPSTEIN-BARR VIRUS-SPECIFIC CYTOTOXIC T-CELL CLONES RESTRICTED THROUGH A SINGLE HLA ANTIGEN.

Wallace LE, Rickinson AB, Rowe M, Epstein MA
Dept. Pathology, Univ. Bristol Medical Sch., Univ. Walk, Bristol BS8 1TD, England
Nature; 297(5865):413-415 1982

Epstein-Barr (EB) virus-specific human cytotoxic T-cell clones, recognizing the virus-induced lymphocyte-detected membrane antigen (LYDMA) in association with one particular human leukocyte antigen (HLA)-A or -B determinant, were established in vitro. T-cells were prepared by in vitro reactivation from seropositive donor SW (HLA-A11, AW24, B7, and BW35) cells. Strong killing of the autologous cell line was not accompanied by any significant reactivity against EB virus

genome-negative human leukemic cell lines HSB2 and K562, which were included as indicators of natural killer-like activity. Lysis of allogeneic EB virus-transformed cells was particularly strong when associated with either HLA-A11 or BW35 antigen matching, and progressively weaker with matching through B7 and AW24. Samples of effector cells were cloned and analyzed. Tests with clone C2 suggested specificity for the viral antigen LYDMA in association with HLA-A11. Clone C2 killed 8/8 EB virus-transformed cell lines from donors typed HLA-A11, but did not kill any of 15 corresponding lines from A11-negative donors. No lysis of EB virus genome-negative target cells was observed. Clone G13 and H8 showed similar results, while clone G9 gave a different pattern of reactivity, suggesting specific recognition of LYDMA in association with HLA-BW35. Clone G9 killed 9/10 EB virus-transformed target cell lines from donors typed HLA-BW35 but none of the 11 corresponding lines tested from BW35-negative donors or any of the relevant EB virus genome-negative target cells. The mechanisms for the observed reactivities are discussed. (24 Refs)

### 23. A HUMAN THY-1-LIKE ANTIGEN EXPRESSED ON CULTURED LEUKEMIC T-CELLS.

**Saji F, Tanigaki N**
**(c/o Tanigaki) Dept. Molecular Immunology, Roswell Park Memorial Inst., Buffalo, NY, 14263**
**Immunogenetics; 15(6):551-563 1982**

A human cell membrane antigen that is highly T-cell specific among a number of leukocyte cell lines was isolated from cells of a human T-cell leukemia cell line, SKW-3. In addition to the high specificity to T-cell-type cell lines, the isolated antigen showed the following characteristics: (1) It is an acidic glycoprotein of approximately 30,000 daltons that has a charge heterogeneity and probably a disulfide bond(s); (2) Its antigenicity is stable when treated with heat, acid, and various protein denaturants; (3) It is widely distributed in lymphoid and nonlymphoid tissues but is most predominant in brain. These features are similar, if not identical, to those reported for the Thy-1 antigen of mouse or rat and have raised the possibility that this cell membrane antigen may correspond to human 'lymphocyte' Thy-1 antigen, the counterpart of human 'brain' Thy-1 antigen. (Author abstract) (28 Refs)

### 24. STRUCTURAL CHARACTERIZATION OF THE HUMAN T CELL SURFACE ANTIGEN (P67) ISOLATED FROM NORMAL AND NEOPLASTIC LYMPHOCYTES.

**Fox RI, Harlow D, Royston I, Elder J**
**Dept. Clinical Res. and Immunopathology, Scripps Clinic and Res. Foundation, 10666 North Torrey Pines Road, La Jolla, CA, 92037**
**J Immunol; 129(1):401-405 1982**

A 67,000-dalton glycoprotein (p67) on normal and neoplastic T cells is defined by reactivity with a monoclonal antibody (antibody SC1) derived against human T chronic lymphocytic leukemia (T-CLL) cells. This antigen is present on greater than 90% of normal thymocytes, normal peripheral blood (PBL) T cells, T acute lymphoblastic leukemia (T-ALL), T-CLL, and B cell chronic lymphocytic leukemia (B-CLL). It is absent from normal B cells, B cell lines, myeloid cells, and stem cell precursors. By using immunoprecipitation of 125I-labeled glycoprotiens and chymotrypsin digestion, the peptide maps of p67 from normal and leukemic lymphocytes revealed that the antigen is highly related among these cell sources, but at least two major forms of the molecule could be identified. One form was prevalent on the T-ALL-derived cell line 8402 and a second form on cell line HPB-T ALL. Peptide maps of PBL from a normal patient, from a T-ALL patient, and from a B-CLL patient were similar to HPB-T ALL cells. In addition to the two major forms of p67, subtle shifts in certain peptides were noted in lymphocytes from each source. The peptide fingerprints of p67 were similar to those obtained from murine Lyt-1 antigen, suggesting possible homology, and were distinctly different from those of murine gp70. Sequential immunoprecipitation experiments verified that the p67 antigen is carried on the same molecule recognized by other independently derived monoclonal antibodies including SC1, L1F12, T101, and OKT1. Cross-blocking experiments indicated that preincubation with antibody L17F12 or T101, but not OKT1, could block subsequent binding of biotin-conjugated antibody SC1. Thus, four of five monoclonal antibodies derived by separate immunizations recognize identical or closely located antigenic sites on p67. (Author abstract) (28 Refs)

### 25. A MONOCLONAL ANTIBODY RECOGNIZING A HUMAN THYMUS LEUKEMIA-LIKE ANTIGEN ASSOCIATED WITH B2 MICROGLOBULIN (MEETING ABSTRACT).

**Knowles RW, Bodmer WF**
**Imperial Cancer Research Fund, London, England**
**Eighth Annual Meeting of the American Association for Clinical Histocompatibility Testing, April 25-29, 1982, San Francisco, California. American Association for Clinical Histocompatibility Testing 41 pp., 1982.**

A monoclonal antibody, M241, was produced which binds to a human cell surface molecule with properties similar to the murine thymus leukemia (TL) antigen. This human TL-like antigen was found on thymocytes and some T cell lines derived from patients with acute lymphocytic leukemia, but was not found on peripheral blood lymphocytes or B cell lines. The monoclonal antibody M241 was used to immunoprecipitate a molecule from lysates of 125I surface labeled MOLT 4 cells which had two subunits, a 43,000 molecular weight chain and a 12,000 molecular weight chain. The small subunit was shown to be Beta2-microglobulin (beta2-m) by immunoprecipitation with a monoclonal antibody, BBM.1, which recognizes human beta2-m. The TL-like molecule recognized by M241 was shown to be serologically distinct from the HLA-A,B,C molecules recognized by three antibodies W6/32, PA2.6 and BB7.8, and distinct from another human thymocyte antigen, the 49,000 molecular weight HTA 1 molecule, recognized by the monoclonal antibody NA1/34. Following removal of thr HLA-A,B,C molecules, the HTA 1 molecules, and the M241 defined TL-like molecules from MOLT 4 lysates, additional beta2-m associated molecules were immunoprecipitated with BBM.1. These molecules contained a 45,000 molecular weight subunit attached to beta2-m. (no Refs)

### 26. A CLONED CELL LINE, MK1, POSSESSING IA ANTIGENS AND ACCESSORY CELL ACTIVITY.

**Kyoizumi S, Noro N, Teshigawara K, Sakaguchi S, Masuda T**
**(c/o Masuda) Inst. Immunology, Faculty Medicine, Kyoto Univ., Yoshida, Konoe, Sakyo, Kyoto 606, Japan**
**J Immunol; 128(6):2586-2594 1982**

A new cell line, termed Mk1, was established by subcloning from M1+ cells derived from murine myeloid leukemia cell line cells, M1-, by coculture with conditioned medium containing a differentiation factor harvested from secondary cultures of embryonic fibroblasts. Mk1 cells, consisting of five clones (A to E), are dish-adherent cells with a few long processes and are nonspecific esterase-positive. These cell line cells have been maintained in the absence of conditioned medium. The capac-

ity to ingest latex particles is low in Mk1 cells, but is significantly higher in both M1+ and Mm1 cells, the latter of which is a clonal subline of M1-cells. Fc receptors for IgG are always observed on 60 to 70% of each Mk1 cell clone, as well as on M1+ and Mm1 cells. Nevertheless, the phagocytic activity for EA (IgG antibody-sensitized sheep erythrocytes) is remarkably low in Mk1 and M1+ cells in comparison to Mm1 cells. Another marked difference between Mk1 and Mm1 cells is the expression of Ia antigen; Ia antigens detected by anti-Iaq and anti-Iak are found in the former, but not in the latter. The expression of Ia antigen in MK1 cells is dependent on the cell cycle, and is accompanied by the appearance of accessory cell activities for lymphocytes in primary and secondary anti-SRBC PFC responses as well as with the production of monokines that substitute for A cells in secondary anti-SRBC PFC responses and augment Con A responses of syngeneic thymocytes. Despite the expression of Ia antigens, Mk1 cells lack the ability to stimulate allogeneic lymphocytes in MLR, suggesting that either Ia on MK1 cells is different than that on other effective stimulator cells or that Mk1 cells lack additional features that contribute to MLR stimulation. Thus, Mk1 and Mm1 cells seem to be counterparts in the macrophage lineage; Mk1 cells as a model of A cells that are poorly phagocytic and Ia antigen-positive, and Mm1 cells as a model of scavengers that are highly phagocytic and lack A cell activity. (57 Refs)

## 27. MOLECULAR WEIGHT DETERMINATION OF TWO GENETICALLY LINKED CELL SURFACE MURINE ANTIGENS: THB AND LY-6.

**Matossian-Rogers A, Rogers P, Ledbetter JA, Herzenberg LA**
**Dept. Immunology, London Hosp. Medical Coll., Turner St., London E1. 2AD, England**
**Immunogenetics; 15(6):591-599 1982**

Various murine tumor lines were screened by FACS analysis for the surface antigens ThB and Ly-6.2. Positive cell lines were used for immunoprecipitation studies. A monoclonal ThB-specific antibody immunoprecipitated a unique acidic protein of approx 16,000 daltons from several positive tumors and from concanavalin A (Con-A) and LPS activated splenic lymphocytes. Monoclonal Ly-6.2-specific antibody was used to immunoprecipitate a 33,500 dalton protein that was shown to exist in four similarly sized forms with different basic charges. In the course of these studies, the apparent molecular weight of the surface antigen T30, immunoprecipitated with a monoclonal T30-specific antibody from the cell line EL4, was found to be approx 25,000 daltons. (Author abstract) (15 Refs)

## 28. STUDIES OF THE FUNCTIONAL PROPERTIES OF ALLOSPECIFIC DR ANTIGEN EXPRESSED ON MELANOMA AND LANGERHANS CELLS AS STIMULATORS OF PRIMARY ALLOGENEIC PROLIFERATIVE AND CYTOLYTIC RESPONSES (MEETING ABSTRACT).

**Pollack MS, Chin-Louis J, Safai B**
**Sloan-Kettering Institute for Cancer Research, New York, NY**
**Eighth Annual Meeting of the American Association for Clinical Histocompatibility Testing, April 25-29, 1982, San Francisco, California. American Association for Clinical Histocompatibility Testing 41 pp., 1982.**

We have previously shown that most cultured human melanoma cell lines and all epidermal Langerhans cells express HLA-DR alloantigens that have the same serological specificities as peripheral blood B-lymphocytes from the melanoma cell or Langerhans cell donors and that allogeneic lymphocyte proliferative responses can be induced by all these cell types. Further studies now indicate that the induction of proliferative responses by both melanoma cells and Langerhans cells do not require the presence of monocytes. Highly purified E-rosette positive T cells which not not contain any detectable M-? positive monocytes show even higher proliferative responses than do unseparated mononuclear cells. However, melanoma and Langerhans cells also show significant differences in relation to the functional expression of their DR determinants. Whereas DR positive melanoma cells show much weaker stimulation of proliferative responses by allogeneic lymphocytes than normal B-cells, freshly isolated Langerhans cells show much stronger stimulation. Also, although reduced stimulation in cases of stimulator cell-responder cell DR matching and the blocking effects of monoclonal and allospecific anti-DR antisera indicate that the DR antigens are highly associated with the proliferation stimulating structures of melanoma cells, Langerhans cells and peripheral blood-B lymphocytes, stimulation by the DR positive melanoma cells leads, in some cases, to the development of melanoma specific cytolytic responses but does not lead to the generation of cytotoxic effector cells directed against either HLA-A,B or HLA-DR target antigens of either the stimulating melanoma cells or HLA matched lymphocytes. These results provide additional evidence for the distinction of the serologically defined HLA-DR antigens from the HLA-D determinants that are defined by functional studies in mixed cell cultures. (no Refs)

## 29. NATURALLY CYTOTOXIC CELLS IN THE RAT: PHENOTYPE OF THE CELLS MEDIATING NATURAL CYTOTOXICITY AND A COMPARISON WITH CELLS MEDIATING ANTIBODY DEPENDENT CYTOTOXICITY (MEETING ABSTRACT)

**Cantrell DA, Robins RA, Brooks CG, Baldwin RW**
**Cancer Research Campaign Laboratories, Unversity of Nottingham, Nottingham NG7 2RD, England**
**Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.**

The fluorescence activated cell sorter was used to separate rat spleen cells into subpopulations with and without the antigens defined by W3/13, W3/25, OX6 and OX8 monoclonal antibodies. The resultant populations were then assayed for NK (natural killer) and ADCC (antibody dependent cellular cytotoxicity) activity in a quantitative 6 hour 51Cr release assay. The data establish that rat NK and ADCC effector cells are heterogeneous with respect to surfaoe antigen expression and that subsets label with W3/13 and OX8 but not W3/25 and OX6 monoclonal antibodies. Despite this heterogeneity, NK and ADCC activity could not be dissociated by W3/13 and OX8 antibodies. Also, there was no evidence that NK cell heterogeneity was related to target cell specificity since in the rat, the data demonstrate that those NK cells which kill solid, leukemic and non neoplastic cells are identical on the basis of the surface markers examined. (no Refs)

## 30. SELECTIVE BLOCKADE OF HUMAN NATURAL KILLER CELLS BY A MONOCLONAL ANTIBODY.

**Newman W**
**Program in Basic Immunology, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104**
**Proc Natl Acad Sci USA; 79(12):3858-3862 1982**

A murine monoclonal antibody, 13.1, which blocks human natural killer (NK) cell-mediated lysis, has been developed. Hybridoma 13.1 was derived by fusion of NS-1 cells with spleen cells from mice immunized with an enriched population

of NK cells. Supernatants of growing hybridomas were screened for their ability to block NK cell-mediated lysis of K562 targets. Antibody 13.1 is an IgG1 with a single light chain type and it does not fix complement. The 13 1 antigen is expressed on all peripheral blood mononuclear cells, with an antigen density approx 1/30th that of HLA antigen heavy chain. Pretreatment and washing experiments revealed that inhibition of cytotoxicity occurred at the effector cell level only. Significant blocking was achieved with nanogram quantities of antibody and was not due to toxic effects on NK cells. Likewise, controls with other antibodies of the same subclass demonstrated that blocking was not a consequence of mere binding to NK cells. When a panel of 17 NK cell-susceptible targets was tested, the lysis of only 5 of these was blocked, namely K562, HL-60, KG-1, Daudi, and HEL, a human erythroleukemic cell line. The lysis of 12 human B cell and T cell line targets was not inhibited. In addition to the demonstration that the 13.1 antigen is a crucial cell surface structure involved in NK lysis, a heterogeneity of target cell recognition has been revealed that argues for the proposition that individual NK cells have multiple recognitive capabilities. (Author abstract) (28 Refs)

## 31. STUDIES OF HUMAN NATURAL KILLER CELLS. II. ANALYSIS AT THE SINGLE CELL LEVEL.

**Rubin P, Pross HF, Roder JC**

**Dept. Microbiology, Queen's Univ., Kingston, Ontario K7L 2V7, Canada**

**J Immunol; 128(6):2553-2558 1982**

This report deals with the nature of conjugate-forming and lytic conjugate-forming lymphocytes, their relationship to natural killer (NK) cells, and the use of the lytic conjugate-forming cell (LCFC) assay with K562 as a measure of NK frequency in normal donors and cancer patients. Conjugate-forming cells (CFC) from granulocyte- and monocyte-depleted peripheral blood were found to be a heterogeneous population of lymphocytes that included cells forming E rosettes (T cells), EA rosettes (Fc receptor-positive cells), and cells positive for OKT3, OKT4, Mac-1, OKM1, and HNK-1. Very few surface immunoglobulin-positive cells were CFC. The CFC population was twofold to threefold enriched in cells positive for the monocyte/null cell markers OKM1 and Mac-1 and the NK cell marker HNK-1. Analysis of the LCFC showed a highly significant correlation between NK1 cytotoxicity and LCFC frequency, leading to the conclusion that LCFC are indeed NK cells, and that the frequency of LCFC vs K562 is an accurate measure of NK cell frequency. Comparison of NK frequency vs overall cytotoxicity of a group of well-defined normal donors indicated that the characteristic level of NK activity seen for different individuals was primarily due to differences in NK frequency. Two examples of abnormal NK function in patients were used to illustrate the potential of the technique. Both patients had markedly reduced cytotoxicity per effector cell, one with a comparatively high NK frequency in association with T gamma proliferation, and the other, a patient on immunosuppressive drugs, with a normal NK frequency. The combination of assays to measure NK frequency and overall NK cytotoxic activity will permit a better understanding of NK function in vivo. (Author abstract) (31 Refs)

## 32. NATURAL CELL-MEDIATED CYTOTOXICITY AS A POSSIBLE ANTI-TUMOUR SURVEILLANCE MECHANISM (MEETING ABSTRACT)

**Stutman O**

**Cellular Immunology Section, Memorial Sloan-Kettering Cancer Center, New York, NY**

**Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.**

Natural cell-mediated cytotoxicity (NCMC) is detected in normal animals as the capacity of their lymphoid cells to lyse a variety of tumor cells in vitro. Based on surface antigen characteristics, genetic control as well as other properties, two major types of effector cells have been described: natural killer (NK) and natural cytotoxic (NC) cells. Both types do not appear to belong to any conventional lymphoid or hemopoietic cell lineage. One of the original differences, ie the preference of the former for lymphoid tumors and of the latter for solid tumors is not that general, since using either resting or boosted (with poly-IC) effector cells, almost all the possible permutations can be detected if enough targets are studied (ie solid tumors lysed exclusively by resting or boosted NK cells, solid tumors lysed by resting NC and boosted NK, etc). This is not surprising since 'NK susceptible' and 'NC susceptible' targets share 'antigenic' determinants based on either cold-target inhibition studies or by the capacity of monosaccharides to block NCMC in vitro. The fact that NCMC exists at relatively high levels in normal animals and does not need time consuming activation like the more conventional immune responses, that the system can deal preferentially with small numbers of tumor cells and that it is independent of conventional 'tumor associated' antigens, make NCMC a likely candidate for exerting immunosurveillance in vivo, in the sense defined by Burnet. (no Refs)

## 33. ULTRASTRUCTURE OF HUMAN NATURAL KILLER CELLS: NATURE OF THE CYTOLYTIC CONTACTS IN RELATION TO CELLULAR SECRETION.

**Carpen O, Virtanen I, Saksela E**

**(c/o Saksela) Dept. Pathology, Univ. Helsinki, Haartmaninkatu 3, 00290 Helsinki 29, Finland**

**J Immunol; 128(6):2691-2697 1982**

The ultrastructure of human NK cells, NK/target cell conjugates and the effect of monensin, a secretion inhibitor, were studied. Human peripheral blood lymphocytes, highly enriched (75 to 85%) in large granular lymphocytes (LGL), which are known to be the mediators of human NK activity, were used as effectors, and K562 cells as targets. LGL-type of cells were characterized in electron microscopy by a low nucleocytoplasmic ratio, indented nucleus, several large mitochondria, prominent Golgi apparatus, and cytoplasmic osmiophilic granules bound by a unit membrane. Their surface was of intermediate villous type. Two types of effector/target contacts were seen: either effector cell protrusions were pushed deep into pouches and lacunae of the target cell surface, or a wide area of intimate cell-to-cell contact was formed. The contact formation was followed by polarization of the effector cell Golgi apparatus towards the contact area. Monensin, a carboxylic ionophore, which interrupts the vesicular traffic of Golgi-derived vacuoles to the cell surface, caused an accumulation of cytoplasmic vesicles in the LGL but had no effect on the effector/target contact formation. Monensin inhibited the NK lysis apparently via cessation of secretion by the LGL. It did not affect the viability of the effector cells. The lytic steps of human NK cells thus involve binding to the target cell, polar-

ization of cytoplasmic organelles towards the target, and apparently a precisely directed exocytosis of secretory material. (Author abstract) (32 Refs)

## 34. PROPAGATION OF MOUSE CYTOTOXIC CLONES WITH CHARACTERISTICS OF NATURAL KILLER (NK) CELLS.

Kedar E, Ikejiri BL, Sredni B, Bonavida B, Herberman RB
Lab. Immunodiagnosis, NCI, Bethesda, MD, 20205
Cell Immunol; 69(2):305-329 1982

Splenocytes obtained from normal mice (BALB/c nude, BALB/c, C3H, C57Bl/6) and from mice bearing lung or pulmonary carcinomas were propagated for 1-12 mo in the presence of crude or mitogen-depleted T-cell growth factor (TCGF). Clones from several TCGF-propagated lymphoid cell lines were established by limiting dilution or the soft agar techniques. All the cultured lines and the majority of the clonal populations derived from them exhibited strong cytotoxic activity in vitro (51Cr release assay) toward a variety of syngeneic and allogeneic tumor target cells, both freshly obtained and passaged in culture, and both lymphoid and solid in origin, and including targets usually resistant to fresh NK cells. Considerable cytotoxic activity was also observed with several rat and human cultured tumor lines. Only low cytotoxic activity was detected against normal lymphoid mouse cells. Cloned populations generally exhibited more restricted target cytotoxicity than the parental cultured lines, and the pattern of reactivity varied among the clones. Of the clones tested for surface markers, all were positive for Thy 1.2, T200, and asialo GM1 and had strong binding to peanut agglutinin, all had undetectable receptors for IgG or IgM, and some were positive for Lyt 2. The cytotoxic activity was augmented by pretreatment of the effector cells with interferon and inhibited by the presence of mannose or galactose during the assay. Several clones were capable of mediating antibody-dependent cellular cytotoxicity and lectin-induced cellular cytotoxicity, and produced relatively large quantities of interferon and lymphotoxin-like material. The findings indicated continuous culturing in TCGF of previously antigen-nonstimulated mouse lymphocytes selects for the growth of at least two distinct populations with activated NK activity, one reacting preferentially with lymphoid tumor target cells, and the second reacting effectively with both lymphoid and solid tumor targets. Both populations have several features of both T lymphocytes and NK cells. (Author abstract) (48 Refs)

## 35. STUDIES ON THE MECHANISM OF NATURAL KILLER (NK) CELL-MEDIATED CYTOTOXICITY (CMC). I. RELEASE OF CYTOTOXIC FACTORS SPECIFIC FOR NK-SENSITIVE TARGET CELLS (NKCF) DURING CO-CULTURE OF NK EFFECTOR CELLS WITH NK TARGET CELLS.

Wright SC, Bonavida B
Dept. Microbiology and Immunology, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA, 90024
J Immunol; 129(1):433-439 1982

It was recently demonstrated that PHA-stimulated murine spleen cells will release soluble natural killer cytotoxic factors (NKCF) selective for NK target cells. The cytotoxic activity of NKCF directed against YAC-1 target cells can be detected by trypan blue uptake after an incubation period of 24 to 48 hr. The role of NKCF in NK cell-mediated cytotoxicity (CMC) reactions was investigated by determining whether the functional characteristics of NKCF conform with the known characteristics of NK activity as defined in the 51Cr-release assay. The following lines of evidence demonstrate that NKCF meet several criteria required to establish their possible role in the lytic mechanism of NK CMC. (1) NKCF are released by murine spleen cells during co-culture with NK-sensitive target cells over an incubation period of up to 48 hr. (2) The effector cell that releases NKCF is Thy-1.2 negative and asialo-GM1 positive. (3) Spleen cells from nude mice released high levels of NKCF, whereas mutant beige (bg/bg) mouse spleen cells release low levels. (4) NKCF lyse only NKA and NKB target cells (YAC-1, RL male 1, FLD-3, and WEHI-164) and non NK-resistant target cells (P815, EL4, AKSL2, R1.1, Molt-4, K562, and Raji). (5) The NK-sensitive YAC-1 cells absorb NKCF more effectively than the NK-resistant EL4 or AKSL2 cell lines. Taking available data of the NK CMC system and the characteristics of NKCF into consideration, a model is proposed for NK CMC reactions in which NKCF play an integral role in the lytic step. In this model, the effector cell must be able to recognize the NK-sensitive target and then release NKCF. On the other hand, for lysis to be achieved, the NK target cell must be able to activate the NK effector cell, to adsorb NKCF, and to be lysed by NKCF. (Author abstract) (17 Refs)

## 36. THE EFFECT OF TARGET CELL DIFFERENTIATION ON HUMAN NATURAL KILLER CELL ACTIVITY: A SPECIFIC DEFECT IN TARGET CELL BINDING AND EARLY ACTIVATION EVENTS.

Werkmeister JA, Helfand SL, Haliotis T, Pross HF, Roder JC
Dept. Radiation Oncology, Ontario Cancer Foundation, Kingston Clinic, King St. West, Kingston, Ontario K7L 2V7, Canada
J Immunol; 129(1):413-418 1982

Induced differentiation of K562 and HL-60 cultures was associated with a concomitant decrease in natural killer (NK) susceptibility of these target cells. The erythroleukemic cell line K562 was induced to undergo erythroid differentiation with optimal concentrations of sodium butyrate or hemin, and HL-60, a promyelocytic leukemia cell line, was induced to differentiate along the myeloid series with dimethyl sulfoxide or along the monocytic lineage with 12-tetra-decanoylphorbol-13-acetate. The kinetics of cellular differentiation was closely associated with changes in susceptibility to NK-mediated lysis. Control experiments performed in the presence and absence of inducers and experiments with noninducible target cells suggest that the differentiation-related decrease in NK-mediated sensitivity is due to the nature of the induced target cells and not the agents per se. The differentiation-induced reduction in target cell susceptibility appeared to be largely specific for NK activity, since other mechanisms of cytolysis such as antibody-dependent cellular cytotoxicity, anomalous killing, and monocyte-mediated lysis were not changed compared to the untreated target cells. No differences were found in lectin-induced cytolysis of untreated and differentiated HL-60 cultures, although butyrate-induced K562 cells were less sensitive to this form of cytolysis. Pretreatment of NK cells with interferon resulted in elevated levels of lysis of both untreated and differentiated target cells but did not restore the susceptibility of the differentiated NK resistant (NKR) target cells to that of the untreated parent cell lines. The predominant reason for the lowered NK susceptibility of the induced target cells was a decrease in the NK binding ability of these cells. The NKR-differentiated K562 cultures were defective in inducing superoxide radical generation from Percoll-enriched NK cells. This induction is associated with an early post-recognition event in the NK lytic pathway. Further analysis of the surface molecules lost or

gained during controlled differentiation may lead to a better understanding of NK-target antigens. (32 Refs)

### 37. STIMULATION OF NATURAL CYTOTOXIC ACTIVITY IN MIXED CELL CULTURES AND BY CULTURE SUPERNATANTS CONTAINING INTERFERON.

**Potter MR, Moore M, Morris AG**
**(c/o Moore) Immunology Div., Paterson Lab., Christie Hosp. and Holt Radium Inst., Manchester M20 9BX, England**
**Immunology; 46(2):401-409 1982**

We have previously demonstrated that lymphocyte preparations cultured for 5 days with a number of different mitomycin-C-treated lymphoid cell lines showed increased non-specific (NK-like) cytotoxic activity. We have now examined the activity induced in T- and B-cell-enriched responder populations, prepared by sheep red blood cell (SRBC) rosette separation, and found that increased cytotoxic activity was present mainly in the T-cell-enriched fraction. To investigate whether soluble factors were involved in the mediation of enhanced cytotoxicity, freshly isolated effector cell populations before measurement of cytotoxicity against K562 cells. Effector cells pretreated with supernatants from mixed cell cultures incubated for 2-6 days showed increased cytotoxic activity, the greatest activity being obtained with supernatants from 4 and 5 days co-cultures. Increased activity was observed when effector cells were pretreated for 2, 4 and 18 hr with supernatants from mixed cell cultures, regardless of the nature of the stimulator cell (T- and B-cell derived lines, K562 and normal allogeneic lymphocytes). Active supernatants were produced by T-cell-enriched, but not B-cell-enriched responder populations. Supernatants from mixed cell cultures were also examined for the presence of interferon (IFN) and in general, those mediating large increases in cytotoxic activity also contained significant anti-viral activity. The IFN detected was not neutralized by antiserum to IFN-beta but was partly neutralized by antiserum to IFN-alpha. pH 2 treatment also removed part of the activity while a combination of pH 2 and anti-alpha completely neutralized the activity suggesting the presence of IFN-gamma and IFN-alpha. The candidacy of IFNs as mediators of enhanced cytotoxicity in this system is discussed. (Author abstract) (39 Refs)

### 38. EFFECT OF INTERFERON-SS ON NATURAL KILLER CELLS: ANALYSIS OF THE MECHANISM OF ACTION (MEETING ABSTRACT).

**Schmitz-Drager BJ, Hayakawa M, Ackermann R**
**Urologische Klinik und Poliklinik der Universitat Wurzburg, Wurzburg, W. Germany**
**6. Symposium fur Experimentelle Urologie, April 15-17, 1982, Bonn, W. Germany. German Association for Urology 155 pp., 1982.**

Interferons (IFN) have the ability to stimulate the cytotoxic activity of natural killer (NK) cells. Since NK cells may play a role in the body's defense against tumors, the mechanism of this activation is of interest chiefly in view of the therapeutic applications of IFN. The following investigations analyze the ways in which interferon-ss activates NK cells. Peripheral mononuclear cells (PMC) were isolated from heparinized venous blood of healthy donors by FICOLL-hypaque density gradient centrifugation and incubated on a monolayer of prostatic carcinoma cell line DU 145. The non-adherent PMC were subsequently incubated for 12 h with 1000 IU of IFN-ss/ml medium, and their cytotoxicity against DU 145 determined in a 4 hr $^{51}Cr$ liberation test. In further experiments a second absorption onto DU 145 monolayers occurred after stimulation with IFN-ss. The cytotoxicity of PMC was completely absorbed during incubation of the PMC on tumor cell layers. A subsequent incubation of the non-adherent PMC with IFN produced a rise in NK cell activity to the pre-absorption level. The IFN-generated cytotoxicity is again absorbed by repeated incubation on a DU 145 tumor cell monolayer. Thus it was possible to show that the transformation of immature NK precursor cells into mature NK cells is induced by stimulation of natural cytotoxicity with IFN-ss. Through this transformation structures are formed on the membrane of NK precursor cells which enable the recognition and binding of target cells. (no Refs) (In GER)

### 39. NATURAL AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY IN TUMOR-ADHERENT T LYMPHOCYTES: EXPRESSION OF FC RECEPTORS AND OF A HUMAN T-SUBGROUP-SPECIFIC ANTIGEN.

**Feucht HE, Hadam MR, Lohmeyer J, Frank F, Rieber EP, Riethmuller G**
**Medical Clinic, Univ. Munich, Ziemssenstr. 1, D-8000 Munich 2, W. Germany**
**Scand J Immunol; 15(5):483-492 1982**

Adherence of human lymphocytes to allogeneic tumor cell monolayers was found to depend on the presence of monocytes. Adherent lymphocytes could be separated from tumor cells by treatment with lidocaine followed by nylon wool passage. Tumor-adherent cells (70% E-RFC, 45% Fcgamma-R, 23% Fcu-R, 5% monocytes) exhibited enriched natural killer (NK) activity not only against the tumor cell line used for isolation but also against seven other targets. When T cells were isolated subsequently as E-rosettes by density gradient centrifugation through Percoll, the enrichment in cytotoxicity was even more pronounced. Tumor-adherent T cells were severalfold enriched in both NK and antibody-dependent cell-mediated cytotoxicity (ADCC) activity. However, this enrichment was not paralleled by a concomitant increase in the number of Tgamma cells (tumor-adherent T cells: 17% Tgamma, 40% Tmu; tumor-nonadherent T cells: 12% Tgamma, 60% Tmu). Marked differences could be observed by staining with a monoclonal antibody that was raised against human leukemic Tgamma cells of high NK and ADCC activity. This antibody (T 8-11) stained 60% of tumor-adherent T cells, 20% of nonadherent T cells and 29% of T-cell controls. These results indicate that the spontaneous cytotoxic activity of human T cells resides within a small population, most of which are characterized by a specific surface antigen but not by conventional Fcgamma receptors. (Author abstract) (41 Refs)

### 40. IDENTITY OF EFFECTOR CELLS PARTICIPATING IN THE REVERSE ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY.

**Saxena RK, Saxena QB, Adler WH**
**Natl. Inst. Aging, NIH, 4940 Eastern Ave., Baltimore, MD, 21224**
**Immunology; 46(2):459-464 1982**

Our previous work has shown that antibody-coated mouse spleen cells express enhanced cytotoxic activity against some Fc-receptor-bearing target tumor cells by a mechanism which appears to be similar to an antibody-dependent cell-mediated cytotoxicity (ADCC) reaction with reversed polarity of the antibody bridge (R-ADCC). In this report we have shown that (i) the levels of basal natural killer (NK), ADCC and R-ADCC cytotoxic activities in mouse spleen cells are strongly correlated with each other, (b) simultaneous induction of ADCC and R-ADCC reactions does not result in an additive cytotoxic response, and (iii) YAC cells which do not bear Fc receptors and are highly sensitive to lysis by NK can specifically and com-

petitively inhibit the ADCC and R-ADCC reactions. These results suggest that the R-ADCC reaction may be mediated by the same effector cell population as mediates NK and ADCC reactions against tumor target cells. (Author abstract) (10 Refs)

## CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION

### 41. HUMAN B-CELL NEOPLASMS IN RELATION TO NORMAL B-CELL DIFFERENTIATION AND MATURATION PROCESSES.

Godal T, Funderud S
Lab. Immunology, Dept. Pathology, Norwegian Radium Hosp., Oslo, Norway
Adv Cancer Res; 36:211-255 1982

Functional studies related to human B-cell neoplasias are reviewed. The B-cell system is described, including its immunoglobulin (Ig) gene organization and expression, repertoire expression, surface markers related to B-cell development, and regulation of B-cell function. General features of B-cell neoplasms, the relationships of the neoplasms to B-cell development, clinical prognosis determinants, and subsets and neoplasms in the B-cell compartment are discussed. Topics discussed include simultaneous expression of IgM and IgD; expression of surface and other Ig classes and the functions of surface Ig; complement receptors and B-cell differentiation; B-cell proliferation and antibody production; and maturation of B-cell neoplasms. Chronic lymphocytic leukemia (CLL), acute lymphoblastic leukemia (ALL), and non-Hodgkins lymphomas (NHL) are discussed. Both in mouse and man there is considerable evidence for the existence of distinct functional subsets of cells in the B-cell compartment. B-cells are assumed to come from a single lineage, and during most stages of development they have multiple choices for further development, ie, they retain differentiation potential. On this basis a model of neoplastic transformation is proposed to account for the existence of multiple myelomas, NHL, CLL, and ALL. (285 Refs)

### 42. ACTIVATION OF HUMAN BLOOD LYMPHOCYTE SUBSETS FOR CYTOTOXIC POTENTIAL.

Masucci G, Masucci MG, Klein E
Dept. Tumor Biology, Karolinska Institutet, S-104 01 Stockholm, Sweden
Cell Immunol; 69(1):21-33 1982

Blood lymphocytes of individuals differ in the spontaneous cytotoxic potential exerted in vitro against certain cell lines (natural killing, NK). In the low NK donors, the activity can be enhanced by short-term IFN pretreatment of the effectors (interferon activated killing, IAK) and by addition of PHA to the short-term assay (lectin-dependent cellular cytotoxicity, LDCC). Lymphocyte subpopulations fractionated on the basis of nylon adherence, SRBC, and EA rosette formation differ in their response to these measures. The results obtained with IFN-treated lymphocytes of low NK donors were similar in strength to the spontaneous activity of the high NK donors. Therefore, the distinction between NK and IAK is only operational. The nylon passed E receptor-negative and low-avidity E receptor-positive cells had the strongest NK activity. The subsets can be triggered for enhanced activity by IFN. In the majority of the cases the high-activity E-receptor-positive subset which did not sediment with EA indicators had low NK effect and was not triggered by IFN. Addition of PHA to the lytic assay, however, induced activity in the subset. Realization of DNA synthesis was not necessary for the lytic performance. The PHA-imposed triggering event was not dependent on IFN production nor on induction of the competence for IFN response. The results showed that all non-B lymphocyte subsets separated on the basis of nylon wool adherence, SRBC, and EA rosetting contain cells with lytic potential if the appropriate stimulus is used. The relative activities of the subsets against K562 and Daudi differed. Cells which rosetted readily with EA indicators had weak effect against Daudi. (Author abstract) (38 Refs)

### 43. HOMOGENEOUS POPULATIONS OF MACROPHAGES FROM HISTIOCYTIC LYMPHOMA PATIENTS AS A SOURCE OF MACROPHAGE SUBPOPULATIONS WHICH DIFFER IN IMMUNOREGULATORY PROPERTIES.

Lavie G, Shoenfeld Y, Shaklai M, Aderka D, Pick AI, Pinkhas J
(c/o Shoenfeld) Dept. Internal Medicine D, Beilinson Medical Center, Petach Tigra, H 9100, Israel
Cancer; 50(1):69-77 1982

The existence of subpopulations of macrophages which express a variety of regulatory activities of other branches of the immune system is suggested in a comparative study of a human macrophage long term culture ZI and a macrophage cell line DAB-1. Both cell cultures were derived from pleural effusions of patients with diffuse histiocytic lymphoma. DAB-1 cells were found to secrete factors which strongly suppress the response of normal T and B lymphocytes to the mitogens PHA, Con-A and pokeweed mitogen (PWM) (by 96-98%) and to stimulate the cytotoxic activity of NK cells. ZI cells secrete factors which have a mild inhibitory effect on the response of lymphocytes to the T-cell mitogens PHA and Con-A and a stimulatory effect on the response to PWM, whereas very little effect could be detected on the activity of NK cells. While DAB-1 cells form large clusters during growth in culture, and are capable of inducing the formation of lymphocyte rosettes around the tumor cells, ZI cells grow as a homogeneous monolayer and could not be shown to form such rosettes. The differences in the behavior of the two cell populations suggest that the malignant transformation may have affected different subsets of macrophages in each case. Cells from histiocytic lymphoma patients may therefore be a source for homogeneous subpopulations of macrophages and their isolation and propagation in culture is one approach by which such subsets can be defined characterized and classified. The biological characterization of macrophage subsets may also be of clinical importance since a transformed subset with broad suppressor activities may lead to a violent and rapidly deteriorating course of disease, as was in the case of the patient from whom the DAB-1 cell line was derived. (Author abstract) (31 Refs)

### 44. LYMPHOKINES: A FORUM FOR IMMUNOREGULATORY CELL PRODUCTS. VOLUME 3. LYMPHOKINES IN MACROPHAGE ACTIVATION.

Pick E, Landy M
Dept. Human Microbiology, Sackler Sch. Medicine, Tel-Aviv Univ., Ramat-Aviv, Tel-Aviv, Israel
Lymphokines 3: 450 pp., 1981.

The role of lymphokines (LK) in macrophage activation (MA) is discussed under the following headings: an introduction to MA, biochemical properties of activated macrophages, enhancement of phagocytosis-associated oxidative metabolism

as a manifestation of MA, macrophage plasma membrane enzymes as differentiation markers of MA, a developmental concept for the heterogeneity of macrophages in response to LK and other signals, role of colony-stimulating factors as primary regulators of macrophage functions, lipopolysaccharide-unresponsive mice as a model for analyzing LK-induced macrophage differentiation in vitro, MA and resistance to intracellular infection, the role of cyclic nucleotides in the suppression of intracellular replication of Toxoplasma in LK-activated macrophages, cytotoxicity of activated macrophages for the multicellular parasite Schistosoma mansoni, the role of LK in granulomatous inflammations, the cytostatic and cytocidal effects of macrophages and their specificity for tumor cells, the killing of syngeneic tumor cells by guinea pig macrophages activated in vitro with lymphocyte mediators, tumor cytotoxicity by LK-activated macrophages: development of macrophage tumoricidal activity requires a sequence of reactions, induction of tumoricidal capacities in mouse and rat macrophages by LK, MA to cytotoxicity by the macrophage cytotoxicity (activating) factor, the effect of activated macrophages on tumor growth in vitro and in vivo, and requirement of transmethylation reactions for immune effector function. (1532 Refs)

## EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS

### 45. MODE OF ACTION OF POLYETHYLENE GLYCOL 6000 IN POTENTIATING THE IN VITRO GENERATION OF ANTITUMOR CYTOTOXICITY BY MOPC-315 TUMOR BEARER SPLEEN CELLS.

**Mokyr MB, Przepiorka D, Dray S**

**Dept. Microbiology and Immunology, Univ. Illinois at the Medical Center, Chicago, IL, 60612**

**Cancer Res; 42(7):2537-2543 1982**

Some of the possible mechanisms by which polyethylene glycol (PEG) augments the ability of MOPC-315 tumor bearer spleen cells to mediate in vitro antitumor cytotoxicity were evaluated. The level of antitumor cytotoxicity obtained in 5-day cultures of tumor bearer spleen cell suspensions correlated inversely with the percentage of Trinitrophenol (TNP)-rosettable cells (presumably metastatic tumor cells) present in the spleen. The kinetics of decrease in the percentage of TNP-rosettable cells coincided with the appearance of antitumor cytotoxicity. In addition, PEG was shown to interfere with the ability of viable tumor cells to suppress the in vitro generation of antitumor cytotoxicity in normal spleen cells cultured with mitomycin C-treated tumor cells. However, the decrease in the content of TNP-rosettable cells and the concurrent increase in the level of antitumor cytotoxicity were not due to direct cytotoxic and/or cytostatic effects of PEG on tumor cells. Spleen cells cultured in the presence of PEG had an increased rate of [3H]thymidine incorporation and proliferation compared to spleen cells cultured in the absence of PEG. However, the PEG-induced decrease in the percentage of TNP-rosettable cells either preceded or occurred at the same time that PEG-induced increase in spleen cell number was observed. Therefore, spleen cell proliferation can at best explain only partially the PEG-induced decrease in the content of TNP-rosettable cells, and other mechanisms for the decrease must be considered. (Author abstract) (25 Refs)

### 46. WHOLE PELVIC IRRADIATION IN STAGE I ENDOMETRIAL CARCINOMA: CHANGES IN NUMBERS AND REACTIVITIES OF SOME BLOOD LYMPHOCYTE SUBPOPULATIONS.

**Onsrud M**

**Tissue Typing Lab., Rikshospitalet, Natl. Hosp., Oslo, Norway**

**Gynecol Oncol; 13(3):283-292 1982**

Peripheral blood lymphocytes of 64 operated, Stage I endometrial carcinoma patients were tested for natural killer (NK) activity, mitogenic (PHA) responsiveness, and distribution of surface markers. Sequential studies showed an 83% reduction of lymphocyte numbers immediately after 4,000 rad whole pelvic irradiation. T cells were relatively more sensitive to in vivo irradiation than NK cells. The long-term effects were studied in patients belonging to a clinical trial and who were either randomized to radiotherapy or not. Three to 5 yr after treatment, the irradiated patients showed increased NK activity and a greater fraction of lymphocytes bearing receptors for the Fc part of immunoglobulin G, as compared to controls. Conversely, lymphocytes from radiotherapy patients showed a depressed PHA responsiveness, which could be attributed to T-cell depletion. When investigated 9-12 yr after treatment, the results of functional tests and cell enumerations were similar for the two treatment groups. It is concluded that this radiotherapy regime causes long-lasting, although transitory, depletions of certain blood lymphocyte subpopulations. On a per cell basis, however, the lymphocytes have retained their functional capacity. (Author abstract) (21 Refs)

### 47. NK ACTIVITY AND ITS RADIORESISTANCE IN LEUKEMIA AND BONE MARROW TRANSPLANTATION (MEETING ABSTRACT).

**Schacter B, Brovall C, Polmar S, Pierce G, Coccia P**

**Case Western Reserve University, Cleveland, OH**

**Eighth Annual Meeting of the American Association for Clinical Histocompatibility Testing, April 25-29, 1982, San Francisco, California. American Association for Clinical Histocompatibility Testing 41 pp., 1982.**

Natural killer (NK) activity may play a role in immune modulation, GVHD (graft verus host disease) and in viral infections. We have evaluated NK activity, and its resistance to gamma irradiation in leukemic patients in remission under evaluation for bone marrow transplantation (BMT) and following engraftment of HLA identical bone marrow. NK activity of peripheral blood mononuclear cells (PBMNC) of 11 patients with acute leukemia was slightly lower than 11 control subjects (x +/- SEM patients: 18.2% +/-4.2%, controls: 27.0% +/-4.1%, p equals .08). Radioresistance of NK activity is controlled by an X linked gene. Ten of eleven patients were radiosensitive by genotyping. Residual NK activity (RA) after 3000 rads of 10 sensitive control subjects was 13.8% +/-1.9% of unirradiated activity; in 10 leukemia patients RA equals 41.7% +/-8.1% (p equals .003) suggesting recruitment of a cell expressing radioresistant NK activity in the leukemics in remission. NK activity and its radiosensitivity was evaluated post-BMT in 9 patients: 7 leukemics, a child with Ewing's sarcoma and a child with SCID (severe combined immunodeficiency disease). The SCID patient, who received without ablation an HLA-A, B, C, D matched buffy coated infusion from a maternal grandfather, showed lymphoid engraftment documented by improved immunological function, marrow and blood karyotype and mild liver GVHD. Conversion of the granulocyte genetic markers did not occur. Conversion of NK radioresistance phenotype did occur. Conversion of NK radioresistance phenotype occurred in 1/2 discordant leukemic recipient/donor

pairs. NK activity and radioresistance in the immediate post-transplant period was evaluated with regard to GVHD and viral infection. In 10 assays of 6 patients, engrafted with sensitive donors, RA of greater than 30% after 3000 rads was positively associated with documented Varicella-Zoster virus (VZV) infection (py less than .025) and not associated with GVHD. NK activity of lymphocytes stimulated in vitro is radioresistant. These data are consistent with the non-myeloid, bone marrow origin of spontaneous NK activity and the recruitment of other cells expressing radioresistant NK activity in leukemia and in VZV infection post-BMT. (no Refs)

### 48. IMMUNE DYSFUNCTION FOLLOWED BY IMMUNOSUPPRESSION AFTER 60CO THERAPY IN PATIENTS WITH MALIGNANT TUMOURS.

Kapoor AK, Tiwari MC, Khan IU, Tandon VK, Tuteja N, Siddiqui JS, Mehrotra RM
Postgraduate Dept. Pathology and Bacteriology and Dept., Radiology K.G. Medical Coll., Lucknow, India
J Indian Med Assoc; 77(3/4):45-48 1981

Twenty-one patients of various morphological type were treated by 60Co teletherapy. During pretherapy period higher mean values of absolute lymphocyte counts (ALC), increased levels of lymphocyte sub-populations (active E, total E, IgFc and murine erythrocyte rosette-forming-cell counts) and elevated levels of serum IgG and IgA were detected in patients. Suppression in values of immunological parameters was observed after 60Co therapy. Initial fall was accompanied with recovery in several parameters. Immunological findings during pretherapy period suggested a defect in immune function. Post-therapy responses initially showed generalized immunosuppression followed by recovery during 5 wk follow-up period. (Author abstract) (15 Refs)

## OTHER RELATED STUDIES

### 49. FUNDAMENTAL MECHANISMS IN HUMAN CANCER IMMUNOLOGY.

Saunders JP, Daniels JC, Serrou B, Rosenfeld C, Denney CB
University of Texas, Graduate Sch. Biomedical Sciences, Galveston, TX
Dev Cancer Res 5: 533 pp., 1981.

Human cancer immunology is considered under the following headings: cell membranes (modulation of complement 3b receptor synthesis on a human B lymphoblastoid cell line, membrane lipids and cellular functions in normal and malignant lymphocytes, tumor cell heterogeneity and blood-borne metastasis, relationship between cell surface thrombin receptors and cytoplasmic microtubules, and other topics), modulation of immune reactions (interferons, adoptive chemoimmunotherapy of murine leukemia with cells secondarily sensitized in vitro and cells numerically expanded by culture with interleukin 2; regulation of natural killer cell activity; specific and non-specific cellular interactions modulating host resistance to tumors; interrelationships between immunoregulatory cells, neoplastic diseases, and immunodeficiency states, and other subjects), surface antigens (possible clinical significance of circulating immune complexes in melanoma patients, natural and activated killer lymphocytes, monoclonal antibodies as probes for cell surface changes in human malignancy, quantitation of isotopic immunoglobulin therapy to tumor-associated proteins, and other topics), tumor surveillance (new approaches to specific and non-specific immunotherapy of established cancer metastases; immunomodulation by nutritional means; specific immune responses to chemically induced tumors; the ability of natural killer cells functions through recognition of glycoconjugates on target cell membranes; in situ, in vitro, and systemic regulation of natural killer cytotoxicity; and characteristics of natural killer cells and their possible role in resistance against tumor growth), and perspectives and prospects. (912 Refs)

### 50. MEDIATION OF CELLULAR IMMUNITY IN CANCER BY IMMUNE MODIFIERS.

Chirigos MA, Mastrangelo MJ, Mitchell M, Krim M
Viruses and Disease Modification Section, Div. Cancer Treatment, NCI, NIH, Bethesda, MD, 20205
Prog Cancer Res Ther; 19:1-275 1982

Among the 25 papers included in this volume are a number of studies on the characteristics of cytotoxicity against a variety of tumor cells (animal and human) by macrophages, natural killer (NK) cells and antibody dependent cellular toxicity (ADCC). Many of the papers have important implications for the possible role of these effector cell mechanisms as mediators of biological response modification. Other subjects treated include: the interrelationships of interferon and interferon inducers to enhance NK cell, and ADCC tumor-lytic effect on animal and human tumors, the relationship of prostaglandins and other immunoregulating agents on feedback inhibition mechanisms and suppressor cells which can modify the immune response. One chapter presents a study undertaken to directly investigate the mechanism(s) whereby cytosine arabinoside influences ADCC activity and Fc receptors. (564 Refs)

### 51. MONOCLONAL ANTIBODIES TO THE P21 PRODUCTS OF THE TRANSFORMING GENE OF HARVEY MURINE SARCOMA VIRUS AND OF THE CELLULAR RAS GENE FAMILY.

Furth ME, Davis LJ, Fleurdelys B, Scolnick EM
Lab. Tumor Virus Genetics, NCI, Bethesda, MD, 20205
J Virol; 43(1):294-304 1982

We have isolated eight rat lymphocyte-myeloma hybrid cell line producing monoclonal antibodies that react with the 21,000-dalton transforming protein (p21) encoded by the v-ras gene of Harvey murine sarcoma virus (Ha-MuSV). These antibodies specifically immunoprecipitate both phosphorylated and non-phosphorylated forms of p21 from lysates of cells transformed by Ha-MuSV. All eight react with the products of closely related ras genes expressed in cells transformed by two additional sarcoma viruses (rat sarcoma virus and BALB sarcoma virus) or by a cellular Harvey-ras gene placed under the control of a viral promoter. Three of the antibodies also react strongly with the p21 encoded by the v-ras gene of Kirsten MuSV. These same three antibodies immunoprecipitate the predominant p21 species synthesized normally in a variety of rodent cell lines, including the p21 produced at high levels in 416B murine hemopoietic cells. This suggests that an endogenous gene closely related to Kirsten-ras is expressed in these cells. The monoclonal antibodies have been used to confirm two properties associated with p21: localization at the inner surface of the membrane of Ha-MuSV-transformed cells, assayed by immunofluorescence microscopy, and binding of guanine nucleotides. (Author abstract) (42 Refs)

## 52. IMMUNOLOGICAL MARKERS.

Matsuno S, Kobari M, Kodera T, Sato T
First Dept. Surgery, Tohoku Univ. Sch. Medicine, Sendai, Japan
Nippon Rinsho; 40(1):51-57 1982

Diagnostic significance of alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), immunosuppressive acidic protein (IAP), pancreatic oncofetal antigen (POA), basic fetoprotein (BFP), and ferritin (F) as tumor markers for hepatic, choledochal, and pancreatic cancer is discussed. AFP and POA are considered to be particularly good markers for liver cancer and pancreatic cancer, respectively, due to the particular characteristics of the organs themselves and the high frequency of the presence of such markers associated with tumors. However, use of these markers alone is not sufficient for early detection of the tumors, so combination assays must be performed. Combining measurements of AFP, BFP, and F for liver cancer, BFP, IAP, and CEA for choledochal cancer, and AFP, BFP, IAP, CEA, and POA for pancreatic cancer was suggested, in conjunction with the leukocyte adherence test, to improve immunological diagnosis of cancer. (23 Refs) (In JPN)

## 53. MONONUCLEAR-CELL INFILTRATION IN OVARIAN CANCER. I. INFLAMMATORY-CELL INFILTRATES FROM TUMOUR AND ASCITES MATERIAL.

Haskill S, Becker S, Fowler W, Walton L
Dept. Obstetrics and Gynecology, Univ. North Carolina, Chapel Hill, NC, 27514
Br J Cancer; 45(5):728-736 1982

Malignant effusions and tumor tissue obtained at surgery provided material for a study of the prognostic value of the various inflammatory cells in the prognosis of human ovarian cancer. Ascitic fluids predominantly contained inflammatory cells; tumor cells, both singly and in clusters, were a minor component. Tumor cells were usually in excess in dispersed solid material. Some patients had significant proportions of lymphocytes and macrophages in their solid tumor, and these patients invariably responded to therapy. Sedimentation-velocity separation at unit gravity provided two populations of inflammatory cells. One consisted of mononuclear cells similar in size to those in the patients blood: the other consisted of one or more large macrophage populations, distinct in morphology and enzymatic markers from both blood monocytes and each other. T lymphocytes were enriched in ascites fractions (78%) and in the tumor-derived mononuclear fraction (71%) compared to patient blood (60%). The T-cell subset characterized by ANAE reactivity was markedly depleted in the tumor-infiltrating fraction (17%) relative to either the ascites (62%) or patient blood (51%). Esterase-positive monocyte-like cells were more frequent in the tumor-infiltrating fraction (17%) than in ascites (7%) or blood (12%). B lymphocytes were infrequent in solid tumors and difficult to assess in ascites. Histiocyte-like macrophages were present in the higher-velocity tumor-cell containing fractions of both solid and ascitic material. The variation in infiltrating cells between patients and between tumor and ascites of the same individual was marked. (Author abstract) (29 Refs)

## 54. MONONUCLEAR-CELL INFILTRATION IN OVARIAN CANCER. II. IMMUNE FUNCTION OF TUMOUR AND ASCITES-DERIVED INFLAMMATORY CELLS.

Haskill S, Koren H, Becker S, Fowler W, Walton L
Dept. Obstetrics and Gynecology, Univ. North Carolina, Chapel Hill, NC, 27514
Br J Cancer; 45(5):737-746 1982

Mononuclear cell fractions were isolated from blood, ascites and solid tumors of patients undergoing surgery for Stages III and IV adenocarcinoma of the ovary, and evaluated for their response in NK, ADCC and PHA assays. Control experiments with the same fraction of normal blood indicated that these responses were not influenced by the enzymes used to isolate the tumor and ascites inflammatory cells. The inflammatory cell fractions isolated from both tumor sites which sedimented in the velocity range of blood mononuclear cells were adequate in number and composition for comparison with similar cells from blood. E RFC values in both ascites and tumor fractions exceeded those of patient blood. However, there was a marked difference in distribution of the T subsets between blood, ascites and tumor, which could cause the variable test results between the different cell sources. PHA responses of patient blood and ascites fractions were about half that of normal blood. Tumor-infiltrating lymphocytes (TIL) were less than 10% as responsive as normal blood. The depressed PHA responses of the TIL were not due to the presence of a suppressor cell population. NK activity of patient blood was less than that of normal blood, but not as much as the ascites or TIL cells. The activity of the ascites-derived lymphocytes was enhanced by treatment with interferon. ADCC activity against both CRBC and SB cells was normal or higher than controls in patient blood, and depressed in the ascites-derived fractions. TIL responded to less than 10% of the patient blood values. The results indicate a lack of response by ascitic and TIL cells in assays dependent on FcR-bearing effector cells and a greater loss of PHA-reactive cells from the tumor than from blood and ascites. These data could result from intratumor inactivation, or a failure of the particular subset to localize either in the ascites or the tumor site. (Author abstract) (32 Refs)

## 55. MONONUCLEAR-CELL INFILTRATION IN OVARIAN CANCER. III. SUPPRESSOR-CELL AND ADCC ACTIVITY OF MACROPHAGES FROM ASCITIC AND SOLID OVARIAN TUMOURS.

Haskill S, Koren H, Becker S, Fowler W, Walton L
Dept. Obstetrics and Gynecology, Univ. North Carolina, Chapel Hill, NC, 27514
Br J Cancer; 45(5):747-753 1982

Macrophages have been isolated from ascitic and collagenase-dispersed tumors from patients undergoing surgery for ovarian cancer. Macrophages were present in varying proportions in both sites, though the ratio of macrophages to tumor cells was higher in ascites. Marked variation in size (as detected by sedimentation velocity) and cytochemical markers in the macrophages was noted. Highly enriched macrophage fractions were isolated from the ascites and collagenase-dispersed solid tumors by a combination of sedimentation velocity and selective EA RFC or adherence techniques. Suppressor activity in the PHA assay was detected in tumor macrophages (4/10 giveing greater than 50% inhibition), ascitic macrophages (1/15) and blood monocytes (2/7). Lymphocyte fractions from tumors were unresponsive to PHA and failed to suppress the blood response. Suppressor activity was also present in the purified tumor-cell fraction of 6/14 patients. ADCC activity was tested in a few patients. When the activity was determined against the SB target cells, tumor-derived macrophages were inactive, whereas the ascitic fraction showed low but significant activity which averaged much lower than patient blood values. The ADCC assays carried out with the CRC target cell indicated activity within the range of patient blood values in 4/4 ascites and 2/4 tumor macrophage fractions. Cytotoxicity was also assessed against co-purified autologous tumor cells. Although activity was detected in many of the tests, the results seemed to reflect target cell sensitivity. There appeared to be a

correlation between cytotoxicity with test macrophages and normal blood mononuclear cells. The results indicate that the cytochemical heterogeneity and the variation in size between macrophage fractions is associated with a spectrum of activities. (Author abstract) (24 Refs)

### 56. LYMPHOCYTE SUBSETS INFILTRATING HUMAN MAMMARY CARCINOMAS (MEETING ABSTRACT)

**Eremin O, Ashley J, Brown M, Williamson S**
**Department of Clinical Surgery, University of Edinburgh, Edinburgh, Scotland**
**Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.**

Lymphocytes infiltrating human mammary carcinomas have been well documented histologically but their precise role in vivo and possible anti-tumor activity has not been defined. Lymphocytes were isolated from primary human mammary tumor using mechanical and enzymatic preparative techniques and cell passage down a sephadex G-10 column. Rosetting techniques were used to characterize both T and B lymphocyte subsets within the tumors. The pattern detected was different, in certain respects, from that found in the blood and suggested a selective subset migration into the tumor. This was confirmed by in vitro cytotoxicity assays revealing an absence of K cells and a paucity of NK cells. The study also established the hyporeactive state (mitogen assays) of the tumor-infiltrating lymphocytes, in contrast to the normal activity of blood lymphocytes. (no Refs)

### 57. YAC-LYMPHOMA BEARING INDUCES FUNCTIONAL CHANGES IN BONE MARROW DERIVED MONONUCLEAR PHAGOCYTES.

**Bursuker I, Shezen E, Goldman R**
**(c/o Goldman) Dept. Membrane Res., Weizmann Inst. Science, 76100 Rehovot, Israel**
**Cancer Lett; 16(1):95-102 1982**

The in vitro differentiation of bone marrow-derived mononuclear phagocytes (BMDMP) showed quantitative and qualitative changes when the donor A/J mice carried YAC-lymphoma cells. Bone marrow cells harvested 4 days after inoculation of animals with either Corynebacterium parvum (CP) or YAC-lymphoma cells expressed enhanced BMDMP colony forming capacity. The lysosomal enzyme marker acid phosphatase was significantly higher in BMDMP differentiated from bone marrow cells harvested from mice bearing YAC-lymphoma than in those derived from bone marrow of control mice, and approx equal to that from those derived from mice treated with CP. At prostaglandin E2 concentrations of 10(-6) - 10(-7) M, the mononuclear phagocyte proliferative capacity of bone marrow cells of control mice was inhibited to a significantly higher extent than that of mice injected with CP or YAC-lymphoma cells. BMDMP from CP-inflamed and YAC-lymphoma bearing mice were more active chemiluminescently than those from control mice. Chemiluminescence activity of BMDMP from YAC-lymphoma bearing mice was lower than that of BMDMP from CP-inflamed mice. (20 Refs)

### 58. JMV MAREK'S DISEASE TUMOR CELLS HAVE B-CELL CHARACTERISTICS.

**Lam KM, Linna TJ**
**Dept. Epidemiology and Preventive Medicine, Sch. Veterinary Medicine, Univ. California, Davis, CA, 95616**
**Clin Immunol Immunopathol; 23(2):527-532 1982**

In vivo and in vitro methods were used to determine whether JMV Marek's disease (MD) tumor cells have B-cell or T-cell characteristics. JMV tumor cells were treated with anti-T-cell serum (ATS) and complement (C) or anti-B serum (ABS) and C and then inoculated into 1-day-old chickens. Within 2 wk of inoculation, 95% of chickens inoculated with ATS- and C-treated cells died of JMV-induced leukemia, whereas only 10% of chickens inoculated with ABS- and C-treated cells succumbed. This in vivo result indicated that the malignant cells may be B cells. In vitro studies corroborated this conclusion. ABS and C killed 99 to 100% of cultivated JMV cells, whereas little or no killing of JMV cells was achieved by ATS and C, as demonstrated by trypan blue dye exclusion or by release of 51Cr from labeled JMV cells. Furthermore, after staining of JMV cells with fluorescein-conjugated rabbit anti-chicken immunoglobulin, all cells fluoresced, indicating that JMV cells have surface immunoglobulin. With support of these lines of evidence, we conclude that JMV Marek's disease tumor cells have B-cell characteristics. (Author abstract) (14 Refs)

### 59. LOSS OF VIRAL GENE EXPRESSION AND RETENTION OF TUMORIGENICITY BY ABELSON LYMPHOMA CELLS.

**Grunwald DJ, Dale B, Dudley J, Lamph W, Sugden B, Ozanne B, Risser R**
**McArdle Lab. Cancer Res., Univ. Wisconsin, Madison, WI, 53706**
**J Virol; 43(1):92-103 1982**

Lymphomas induced by the Abelson murine leukemia virus (A-MuLV) were examined for the expression of biochemical and biological markers associated with A-MuLV transformation before and after in vivo growth in genetically distinguishable host mice. Although all tumors and clonal lines derived from them initially expressed the A-MuLV-encoded gag fusion protein p160, they ceased synthesis of this molecule after several weeks of growth in vivo as ascites tumors. Transplanted clonal lines continued to express the alloantigenic marker H-2b and the isoenzyme marker Gpi-1b of the donor tumor cells, indicating that the cells were of donor and not host origin. Examination of cellular DNA obtained from p160-positive and derivative p160-negative lines indicated that p160-negative clones had lost A-MuLV-specific proviral sequences as detected by hybridization with several probes. Although the clonal lines no longer expressed p160, they retained their malignant phenotype and continued to express the Abelson antigen, a cell surface marker associated with A-MuLV lymphomagenesis. Continued expression of the A-MuLV genome was not required for maintenance of oncogenic potential under these conditions of in vivo tumor growth. (Author abstract) (38 Refs)

# AUTHOR INDEX WITH CITATION NUMBERS


Ackermann R. 38
Aderka D. 43
Adler WH. 40
Andersen BL. 1
Anderson VA. 20
Ashley J. 56
Baldwin RW. 29
Ballester JM. 4
Beardsley T. 13
Becker S. 53
Becker S. 54
Becker S. 55
Bennett P. 15
Benson JD. 3
Bernard A. 11
Bettelheim P. 2
Bodmer WF. 25
Bonavida B. 34
Bonavida B. 35
Boumsell L. 11
Brandrup F. 1
Brooks CG. 29
Brovall C. 47
Brown M. 56
Bursuker I. 57
Cantrell DA. 29
Carnot J. 4
Carpen O. 33
Centurioni R. 10
Centurioni R. 16
Chassagne J. 11
Chin-Louis J. 28
Chirigos MA. 50
Christensen BE. 1
Coccia P. 47
Cruz C. 4
Dale B. 59
Danieli G. 10
Danieli G. 16
Daniels JC. 49
Davis LJ. 51
Davis S. 8
De Bruin HG. 6
Demeocq F. 11
Denney CB. 49
Dray S. 45
Dudley J. 59
Elder J. 24
Epstein MA. 22
Eremin O. 56
Farcet JP. 18
Fellous M. 9
Feucht H. 7
Feucht HE. 39
Fjelde A. 15
Fleurdelys B. 51
Fowler W. 53
Fowler W. 54
Fowler W. 55
Fox RI. 24
Frank F. 39
Funderud S. 41
Furth ME. 51
Gabrielli A. 16
Godal T. 41
Goldman R. 57
Golomb HM. 8
Gordon J. 20
Gourdin MF. 18
Grunwald DJ. 59
Haas M. 13
Hadam MR. 39
Haliotis T. 36
Harlow D. 24
Haskill S. 53
Haskill S. 54
Haskill S. 55
Hayakawa M. 38
Helfand SL. 36
Herberman RB. 34
Hernandez P. 4
Herzenberg LA. 27
Hill S. 13
Hirose M. 12
Huhn D. 7
Ikejiri BL. 34
Im TS. 5
Isaacson P. 14
Jennette JC. 3
Jonasson J. 13
Jones DB. 14
Jonsson V. 1
Kamitani T. 5
Kapoor AK. 48
Kedar E. 34
Kellam J. 15
Khan IU. 48
Kimura Y. 5
Klein E. 42
Knapp W. 2
Knowles RW. 25
Kobari M. 52
Kodera T. 52
Koren H. 54
Koren H. 55
Krim M. 50
Kyoizumi S. 26
Lam KM. 58
Lamph W. 59
Landy M. 44
Lavie G. 43
Ledbetter JA. 27
Lemerle J. 11
Lenoir GM. 9
Leoni P. 10
Leoni P. 16
Lilleyman JS. 17
Linna TJ. 58
Lipinski M. 9
Liszka K. 2
Lohmeyer J. 39
Lohmeyer J. 7
Lum LG. 21
Mahda H. 5
Majdic O. 2
Marchegiani G. 10
Marchegiani G. 16
Mastrangelo MJ. 50
Masucci G. 42
Masucci MG. 42
Masuda T. 26
Matossian-Roger. 27
Matsuno S. 52
Mehrotra RM. 48
Melief CJ. 6
Miedema F. 6
Minato K. 12
Mitchell M. 50
Mokyr MB. 45
Montillo M. 10
Montillo M. 16
Montroni M. 10
Montroni M. 16
Moore M. 37
Morris AG. 37
Newman W. 30
Noro N. 26
Okuda K. 5
Onsrud M. 46
Orcutt-Thordars. 21
Ostenson RC. 21
Ozanne B. 59
Ozer H. 15
Park K. 5
Pattengale PK. 13
Pick AI. 43
Pick E. 44
Pierce G. 47
Pinkhas J. 43
Plagne R. 11
Pollack MS. 28
Polmar S. 47
Potter MR. 37
Pross HF. 31
Pross HF. 36
Przepiorka D. 45
Reyes F. 18
Richard Y. 11
Rickinson AB. 22
Rieber EP. 39
Rieber EP. 7
Riethmuller G. 39
Riethmuller G. 7
Risser R. 59
Robins RA. 29
Roder JC. 31
Roder JC. 36
Rogers P. 27
Rosenfeld C. 49
Rothenborg HW. 1
Rowe M. 22
Royston I. 24
Rubin P. 31
Rumke HC. 6
Safai B. 28
Saji F. 23
Sakaguchi S. 26
Saksela E. 33

Salomon JC ..... 9
Santos MN ..... 4
Sato T ..... 52
Saunders JP ..... 49
Saxena QB ..... 40
Saxena RK ..... 40
Schacter B ..... 47
Schlimok G ..... 7
Schmitz-Drager ..... 38
Scolnick EM ..... 51
Seigneuret MC ..... 21
Serrou B ..... 49
Shaklai M ..... 43
Shezen E ..... 57
Shimoyama M ..... 12
Shoenfeld Y ..... 43
Siddiqui JS ..... 48
Smit JW ..... 6
Sredni B ..... 34
Stevenson GT ..... 20
Storb R ..... 21
Strauchen JA ..... 19
Stutman O ..... 32
Sugden B ..... 59
Sugden PJ ..... 17
Svarch E ..... 4
Sworn MJ ..... 14
Tandon VK ..... 48
Tanigaki N ..... 23
Tatsumi N ..... 5
Tatsumi Y ..... 5
Taylor CR ..... 13
Ten Berge IJ ..... 6
Terpstra F ..... 6
Teshigawara K ..... 26
Tetaud C ..... 9
Thiel E ..... 7
Thomsen K ..... 1
Tiwari MC ..... 48
Tursz T ..... 9
Tuteja N ..... 48
Twomey P ..... 13
Van de Griend R ..... 6
Van der Reijden ..... 6
Vardiman J ..... 8
Viallard JL ..... 11
Virtanen I ..... 33
Von dem Borne A ..... 6
Wallace LE ..... 22
Walton L ..... 53
Walton L ..... 54
Walton L ..... 55
Werkmeister JA ..... 36
Wieis J ..... 9
Wilkman AS ..... 3
Williamson S ..... 56
Wilson C ..... 8
Wright DH ..... 14
Wright SC ..... 35
Yamamoto S ..... 5
Zeijlemaker WP ..... 6

# VIDEOTAPES

## ON CURRENT TOPICS IN CANCER RESEARCH

A pilot project of the International Cancer Research Data Bank (ICRDB) Program of the National Cancer Institute

*Three series are available . . .*

### THE RELATION OF CARCINOGEN ACTION ON DNA TO CELL TRANSFORMATION

| | | |
|---|---|---|
| PETER MAGEE<br>Fels Research Institute | *Keynote Address* | #VK01<br>28 min. |
| JAMES K. SELKIRK<br>Oak Ridge National Laboratories | *Metabolic Activation and Macromolecular Binding of Chemical Carcinogens* | #VK02<br>51 min. |
| PHILIP C. HANAWALT<br>Stanford University | *Cellular Responses to Damaged DNA* | #VK03<br>54 min. |
| CHARLES HEIDELBERGER<br>University of Southern California | *Mutagenesis and Oncogenic Transformation of Mouse Embryo Cells* | #VK04<br>54 min. |
| FRED RAPP<br>Milton S. Hershey Medical Center | *The Interaction of Herpesviruses and Host Cells Leading to Latency or Transformation* | #VK05<br>52 min. |
| | *Panel Discussion* | #VK06<br>31 min. |

### MECHANISMS OF METASTASIS

| | | |
|---|---|---|
| ISAIAH FIDLER<br>Frederick Cancer Research Center | *The Heterogeneous Nature of Cancer Metastasis and Implications for Therapy* | #VB01<br>47 min. |
| GEORGE POSTE<br>Smith, Kline and French Laboratories | *Phenotypic Analysis of Metastatic Cell Populations* | #VB02<br>42 min. |
| LANCE LIOTTA<br>National Cancer Institute | *Tumor Cell Invasion of Basement Membranes and Extracellular Matrices* | #VB03<br>33 min. |
| EVERETT SUGARBAKER<br>Miami Cancer Institute | *Some Clinical Characteristics of Metastasis in Man* | #VB04<br>41 min. |

### AUTOMATED CYTOLOGY

| | |
|---|---|
| Part One: Principles and Techniques | #VB05<br>56 min. |
| Part Two: Biological Applications | #VB06<br>52 min. |

VIDEOTAPES ON CURRENT TOPICS IN CANCER RESEARCH are in the 3/4" U-matic format and can be played on video equipment which accepts the NTSC standard (the standard for videotapes produced in the U.S.). The two Automated Cytology tapes (#VB05 and #VB06) are also available in the PAL format.

The videotapes are available on a loan basis. If you would like to schedule viewing for your group, or for more information, please write to:

Videotape Coordinator
ICRDB Program
Westwood Building, Room 10A18
Bethesda, MD 20205

Please specify three choices for viewing dates, and the tapes desired.

☆ U.S. GOVERNMENT PRINTING OFFICE: 1982-381-847:203

**U.S. DEPARTMENT OF COMMERCE**
**National Technical Information Service**
5285 Port Royal Road
Springfield, Va. 22161

OFFICIAL BUSINESS

Penalty for Private Use, $300

**PRINTED MATTER**

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF COMMERCE
COM-211

THIRD CLASS
BULK RATE

CB-17

**CANCERGRAMS are distributed for the International Cancer Research Data Bank (ICRDB) by the National Technical Information Service (NTIS). CANCERGRAMS are available from NTIS on a standing order basis at $2 each for North American Continent addresses and $3 each for other addresses. An NTIS deposit account is required. For a list of subject categories or other information, please write to:**

**Subscription Section**
**National Technical Information Service**
**5285 Port Royal Road**
**Springfield, VA 22161**

**NOTICE OF MAILING CHANGE**

☐ Check here if you wish to discontinue receiving this publication.

☐ Check here if your address has changed and you wish to continue receiving this publication. (Be sure to furnish your complete address including zip code.)

Tear off cover with address label still affixed and send to:

Computer Support Center
ICRDB Program
IIT Research Institute
10 West 35th Street
Chicago IL. 60616

CB 17/82/12

NCI/ICRDB/CB17 82/12

PB82-931812

# ICRDB CANCERGRAM

# IMMUNOBIOLOGY AND CANCER

## Identification and Characterization of Immune Cells

SERIES CB17 No. 82/12

DECEMBER, 1982

This Cancergram is a service of the INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM of the U.S. National Cancer Institute. Every few weeks, an updated Cancergram containing abstracts of selected cancer-related articles recently published in more than 3000 journals, and dealing with the topic indicated by the above title, is sent to researchers working in this area. These researchers are identified on the basis of the description of their current research project that has been submitted to the ICRDB Program, directly or via granting agencies.

This Cancergram is prepared by the Cancer Information Dissemination and Analysis Center (CIDAC) for Virology, Immunology, and Biology. ***If this Cancergram is useful and valuable, please send your comments to the CIDAC address below, since future editions depend on user satisfaction and user needs:***

NEWARK PUBLIC LIBRARY

DEC 10 1982

U. S. GOVT. PUBS.
DEPOSITORY 376

CIDAC FOR VIROLOGY, IMMUNOLOGY, AND BIOLOGY
SCIENCE INFORMATION SERVICES
FRANKLIN INSTITUTE RESEARCH LABORATORIES
20TH AND RACE STREETS
PHILADELPHIA, PA 19103

*In this issue:*


- CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS ..... 1-13
- DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS ..... 14-17
- LYMPHOCYTE AND DIFFERENTIATION ANTIGENS ..... 18-26
- CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION ..... 27-36
- EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS ..... 37-45
- OTHER RELATED STUDIES ..... 46-60


## CLASSIFICATION OF HUMAN LEUKEMIAS AND LYMPHOMAS BY CELL SURFACE MARKERS

### 1. THE IMMUNOLOGICAL CLASSIFICATION OF LEUKAEMIA BASED ON A RAPID MICROCYTOTOXICITY TEST.

**Billing RJ, Foon KA, Linker-Israeli M**
**1000 Veteran Ave., Los Angeles, CA, 90024**
**Clin Exp Immunol; 49(1):142-148 1982**

We describe a rapid, accurate, and reproducible cytotoxic antibody test for the immunological classification of leukemia. Well characterized heteroantisera and monoclonal antibodies were distributed in a microcytotoxicity tray referred to as a leukemia screening tray (LST). Leukemia cells were tested for the presence of Ia-like, 'blast', thymocyte, common acute lymphoblastic leukemia (cALL), and acute myeloblastic leukemia (AML) antigens. Utilizing this technique, T ALL could be distinguished from non-T ALL, ALL and AML could be differentiated, the myeloid blast crisis of chronic myelogenous leukemia (CML) could be distinguished from the lymphoid blast crisis, and the T lymphocyte and B lymphocyte lymphoid leu-

**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Public Health Service • National Institutes of Health • National Cancer Institute**

HE 20. 3173/2:

kemias were readily identified. It has been shown that subclassification of leukemia according to surface markers, as described here, offers considerable improvement in the diagnosis and treatment of leukemia over the classical morphological methodologies. Because the test can be completed in 2 hr and unlimited amounts of monoclonal antibodies are available, the LST or similar tests should become universally available in the future to supplement morphological data and replace other lengthy enzyme and rosetting tests. (Author abstract) (34 Refs)

## 2. SURFACE MARKERS ON LEUKEMIA AND LYMPHOMA CELLS: RECENT ADVANCES.

**Foon KA, Schroff RW, Gale RP**
**Biological Response Modifiers Program, NCI-Frederick Cancer Res. Facility, Building 560, Frederick, MD, 21701**
**Blood; 60(1):1-19 1982**

Recent advances in immunology have led to important insights into leukocyte differentiation and the cellular origin of leukemia. It is now possible to precisely define stages of human lymphocyte and granulocyte differentiation utilizing highly specific monoclonal antibodies that define cell surface antigens in conjunction with more traditional markers such as surface and cytoplasmic immunoglobulin on B lymphocytes, sheep erythrocyte (E) receptors on T lymphocytes, and cytochemical staining of myeloid cells. Five major subtypes of acute lymphoblastic leukemia (ALL) are now recognized, including unclassified or null ALL, common ALL (cALL), pre-B-ALL, B-ALL, and T-ALL. Within the T-ALL subgroup, there is considerable heterogeneity based on the presence or absence of the E-receptor and various T-cell surface membrane antigens defined by monoclonal antibodies. Cells from patients with chronic lymphocytic leukemia, non-Hodgkin's lymphoma, and Sezary syndrome also can be classified by their reactivity with monoclonal antibodies. Acute myelogenous leukemia (AML) cells are generally classified by morphological and cytochemical features. Recently, monoclonal antibodies reactive with granulocytic and monocytic subtypes of AML have been developed. In addition to their utility in leukemia classification, monoclonal antibodies that identify leukemia associated antigens have also been used therapeutically. Monoclonal antibodies have been infused intravenously into patients with leukemia and lymphoma. They have also been used in vitro with complement to lyse residual leukemia cells from remission bone marrows removed from leukemia patients. These treated bone marrows were later reinfused into the same patients to 'rescue' them following high-dose chemotherapy and radiation therapy. (Author abstract) (203 Refs)

## 3. SEROLOGICAL ANALYSIS OF CELL SURFACE ANTIGENS OF NULL CELL ACUTE LYMPHOCYTIC LEUKEMIA BY MOUSE MONOCLONAL ANTIBODIES.

**Ueda R, Tanimoto M, Takahashi T, Ogata SI, Nishida K, Namikawa R, Nishizuka Y, Ota K**
**Lab. Chemotherapy, Aichi Cancer Center Res. Inst., Nagoya 464, Japan**
**Proc Natl Acad Sci USA; 79(14,part1):4386-4390 1982**

Nine antigen systems were defined. Two were related to HLA-A,B,C and to Ia-like antigens; the others could be grouped into three categories. (i) NL-22, NL-1: NL-22 antibody reacted with leukemia cells from 12 of 16 cases of null cell acute lymphocytic leukemia (null-ALL) but not with any other type of leukemia tested or with lymphoid cells of various origins. Among cultured cell lines tested, one (NALM-6) of three null-ALL cell lines was positive; the others were negative. Absorption analysis confirmed the restriction of NL-22 antigen to null-ALL. NL-1 antibody was reactive with leukemia cells from 10 of 16 cases of null-ALL and 3 of 6 cases of chronic myelocytic leukemia in blastic crisis (CML-BC). The antigen was present also on a minor population of normal lymphoid cells. The distribution and mol wt (100,000; glycoprotein) of the NL-1 antigen resembled that of the previously described common ALL antigen (cALL). (ii) NL-30, NL-4: Both antibodies exhibited almost identical patterns of reactivities against cultured cell lines tested. They reacted with leukemia cells from some cases of null-ALL, adult T-cell leukemia, and CML-BC, although they showed discordance in their reactivities against a panel of leukemia cells. (iii) NL-9, NL-8, NL-25: These three antibodies detect serologically distinguishable determinants on a broad range of leukemias and normal lymphoid and hematopoietic cell types. The antibodies analyzed in this study provide evidence for the heterogeneity of null-ALL by demonstrating a variety of antigen phenotypes on leukemia cells. One of the antigens (NL-22) appears to be restricted to null-ALL. (Author abstract) (27 Refs)

## 4. IMMUNOLOGICAL SUBTYPING OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) USING PEANUT LECTIN (ARACHUS HYPOGEA) (MEETING ABSTRACT).

**Coffey T, Russell EC, Mohanakumar T**
**Medical College of Virginia, Richmond, VA, 23298**
**Fed Proc; 41(3):727 1982**

Childhood ALL is composed of subgroups defined by immunologic markers and certain markers are known to have prognostic significance. Null cell ALL is the largest subgroup and additional markers are needed to identify patients at increased risk of early relapse within this non-T, non-B category. We have used a direct immunofluorescence assay to identify the presence of receptors for the lectin peanut agglutinin (PNA) on blasts from 26/46 (63%) of our null cell ALL patients and have subsequently noted a high rate of relapse (17/26) in the PNA+ group. Relapse has occurred in only 5/20 patients whose blasts lacked the PNA receptor. The PNA+ and PNA- groups were comparable in clinical features (ie, age, leukocyte count, follow-up times) and the striking difference in relapse rate was correlated only with the presence of receptors for the lectin. PNA receptors are commonly found only on fetal thymocytes but not on normal mature peripheral lymphocytes. SDS-PAGE (sodium dodecyl sulfate polyacrylamide gel electrophoresis) analysis of NaB3H4 galactose oxidase labelled solubilized cell membrane extract revealed a 68,000 dalton glycoprotein found only on PNA+ ALL lymphoblasts. Neither PNA- blasts nor PNA+ normal thymocytes expressed this component. The lectin PNA seems to define a high risk group of null cell ALL patients and to be associated with a specific cell membrane component. (no Refs)

## 5. EFFECT OF THYMOSIN FRACTION V ON HUMAN BONE MARROW AND BLOOD CELLS FROM NEWLY DIAGNOSED ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) PATIENTS (MEETING ABSTRACT).

**Narula N, Miller DR, Meyers PA, Pahwa R**
**Memorial Sloan-Kettering Cancer Center, New York, NY, 10021**
**Proc Am Soc Clin Oncol; 1:C-161 1982**

Incubation of normal bone marrow lymphocytes (BML) and peripheral blood lymphocytes (PBL) with thymosin Fraction V (Fr V) results in an increase of certain T-cell markers. In the present study, we investigated the influence of thymosin Fr V on certain surface markers and functions of leukemic cell popu-

lations. Ficoll-Hypaque-separated BML and PBL (comprised of greater than 95% blasts) from 24 patients with ALL (3 of T-cell origin and 21 of non T-non B or Null cell type) were incubated with 25 ucg and 100 ucg of thymosin Fr V for 15 hours. The cells were washed and tested for induction of receptors for peanut agglutinin (PNA), rosette formation with sheep erythrocytes (E-R), surface antigens using monoclonal anti-Ia and anti-T cell (HuLyt 1, HuLyt 2, and HuLyt 3) antibodies and proliferative responses to mitogens phytohemagglutinin, concanavalin A, and pokeweed. Induction of PNA receptors was noted in PBL and BML in one patient and of E-R receptors in four patients. Marked heterogeneity was noted in the expression of Ia and Lyt antigens on the leukemic cells. With thymosin Fr V induction of one or more Lyt antigens occurred in cells of 3 patients (null-ALL). Functional activity was lacking in cells of all patients, and no change was noted after exposure to thymosin. Blasts cells from one patient were lacking in E-rosette forming capacity, while expressing the HuLyt 3 antigen, thus indicating a dissociation between these two markers. This study indicates that T as well as Null cell leukemias as defined by conventional tests can be potentially subclassified on the basis of additional surface markers, and that thymosin Fr V can induce certain T cell markers in so called 'null' type of leukemic cells. (no Refs)

## 6. COLONY-FORMING ASSAY FOR CIRCULATING CHRONIC LYMPHOCYTIC LEUKEMIA CELLS.

**Taetle R, Richardson D, To D, Royston I, Mendelsohn J**
**Univ. Hosp. H720, 225 Dickinson St., San Diego, CA, 92103**
**Leuk Res; 6(3):335-344 1982**

Adaptation of a technique for growth of B lymphocyte colonies to peripheral blood cells of 18 patients with clinically and pathologically typical chronic lymphocytic leukemia (CLL) is reported. T-lymphocyte-depleted CLL peripheral blood cells were cultured with irradiated, normal T cells, and media conditioned by normal, mitogen-stimulated T cells in methylcellulose. Small colonies of approx 40 cells appeared after 5-7 days incubation and little or no growth was noted in the absence of irradiated T lymphocytes. The relationship between the number of cells plated and number of colonies observed was linear over a wide range of plating concentrations. No correlation was observed between plating efficiency and the number of circulating leukocytes or lymphocytes. A high percentage of CLL colony-forming cells were synthesizing DNA (S phase). Cells harvested from normal T lymphocyte colonies were greater than 95% sheep red blood cell-rosette positive and greater than 95% positive when stained for OKT3 and/or T101, compared with less than 5% of cells harvested from CLL colonies. The presence of large numbers of surface immunoglobulin positive cells could not be demonstrated in CLL colonies. Drug sensitivity studies to adriamycin (ADM) and melphalan (ME) were performed on five patients previously treated with alkylating agents and five patients who were untreated. CLL colony-forming cells were relatively resistant to ADM, although untreated patients were less resistant than previously treated ones. Previously treated patients were also relatively resistant to ME. Results indicated that the reported system can be used to study regulation of CLL cell proliferation, and may have utility in predicting response to chemotherapeutic agents. (37 Refs)

## 7. ISOLATION OF MYELOID PROGENITOR CELLS FROM PERIPHERAL BLOOD OF CHRONIC MYELOGENOUS LEUKEMIA PATIENTS.

**Griffin JD, Beveridge RP, Schlossman SF**
**Div. Tumor Immunology, Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115**
**Blood; 60(1):30-37 1982**

Myeloid progenitor cells (colony- and cluster-forming cells in semisolid medium, CFU-GM) were purified from the peripheral blood of chronic myelogenous leukemia (CML) patients. Lymphocytes, monocytes, and most immature myeloid cells were simultaneously depleted with specific monoclonal antibodies using an erythrocyte rosette technique for cell separation. Cells expressing Ia-like antigen were then selected from the residual cell population. Day 7 CFU-GM were enriched 44-116-fold in the Ia+ cell fraction, when compared to the unseparated cells, and up to 47% of the cells could form a myeloid colony or cluster in culture. This cell fraction contained up to 92% undifferentiated blasts, with the remainder mostly promyelocytes. The enriched CFU-GM cells were dependent on an exogenous supply of colony-stimulating factor for growth, and colony formation was linear with cell concentration over a large range (10(4) -10(1) cells/ml). This technique of rosette depletion and enrichment with specific monoclonal antibodies provides a unique method for purifying a homogenous population of myeloid precursor cells with defined surface antigen characteristics. (Author abstract) (50 Refs)

## 8. GALL BODY MARKS T LINEAGE LEUKEMIAS (MEETING ABSTRACT).

**Marcus JN, Hurtubise PE, Quiroga LE**
**Department of Pathology, University of Cincinnati Medical Center, Cincinnati, OH**
**71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-5, 1982, Boston, Massachusetts. International Academy of Pathology 95 pp., 1982.**

Previously we showed that the Gall body (GB), a conspicuous cytoplasmic granule observed supravitally, segregates mainly with mature T helper/inducer lymphocytes, and our preliminary studies suggest it is present as well in thymocytes in most or all maturation stages. Here we extend these observations to neoplastic cells and report that the GB, in parallel fashion, segregates with lymphoid leukemias of thymus lineage. Leukemia cells from 25 patients were studied for T and B cell surface markers, unifocal cytoplasmic acid esterase (FAcE) (an enzyme partially associated with the GB), and the presence of the GB by phase microscopy. Seven leukemias with an appreciable fraction (greater than 15 per cent) of GB+ neoplastic cells were FAcE+, non-B lymphoid types. Two of these were Sezary leukemias in patients with mycosis fungoides and polydispersed hypergammaglobulinemias; the leukemic cells formed E rosettes (E+) and bore T helper cell membrane antigen (OKT4+). Two others were T cell ALLs in young men with mediastinal masses; the cells were E+ and bore combinations of OKT surface T antigens. The remaining three were 'null cell' ALLs in young males; the cells were E- and OKT-. The 18 GB- leukemias averaged only 1.5 per cent GB+ neoplastic cells: 11 were lymphoid (eight FAcE+/- B cell CLLs, one T suppressor OKT8+ CLL, two FAcE+ null-ALLs), three were nonlymphoid, and five were unclassified. (no Refs)

## 9. PHENOTYPE OF CELLS INVOLVED IN MYCOSIS FUNGOIDES AND SEZARY SYNDROME (BLOOD AND SKIN LESIONS): IMMUNOMORPHOLOGICAL STUDY WITH MONOCLONAL ANTIBODIES.

**Schmitt D, Souteyrand P, Brochier J, Czernielewski J, Thivolet J**
**Dept. Dermatology, Hopital Edouard-Herriot, F-69374 Lyon Cedex 2, France**

**Acta Derm Venereol (Stockh); 62(3):193-199 1982**

The phenotypic expression of immunocompetent cells involved in lesions of cutaneous T-cell lymphoma (mycosis fungoides and Sezary syndrome) was studied by using monoclonal antibodies specific for T-cell subsets and HLA-DR antigens (OKT3, T4, T6, T8) (BL 6, BL 5, BL 2). In Sezary syndrome, the phenotype of Sezary cell is homogeneous (T3+, T4+, T8-, T6-, BL2-) and corresponds to the phenotype expressed by the normal helper T-cell population. At the ultrastructural level, the discontinuous distribution of OKT4 and OKT3 antigenic sites on the cell surface is similar to the HTLA antigens. In skin lesions, the Langerhans cells expressed two specificities shared by normal thymocytes (T6 and BL6). We suggest that the expression of these antigens could be related to the epithelial microenvironment (epithelium-dependent differentiation antigens). The tumoral lymphoid cells infiltrating the skin showed the same phenotype (helper type) as the circulating Sezary cells (T3+, T4+, T8-, T6-). Moreover, The T3+ cells also expressed HLA-DR antigens and corresponded to activated T lymphocytes. The various subpopulations of immunocompetent cells seemed to be related to the MHC-derived antigens. (Author abstract) (29 Refs)

## 10. THE INFECTIONS MONONUCLEOSIS DOWNEY CELL POPULATION AND PAUL-BUNNELL ANTIGEN/ ANTIBODY (MEETING ABSTRACT).

**Fjelde A, Roholt O, Kellam J, Bennett P**
**Roswell Park Memorial Institute, Buffalo, NY, 14263**

**Proc Am Assoc Cancer Res; 23:1079 1982**

In conjunction with previous studies with F Milgrom and K Kano, of the Paul-Bunnell (PB) heterophile system, in which we demonstrated presence of PB antigen in (40%) human lymphoma-leukemia (LL) spleens, we studied the abnormal Downey cells found in IM along with PB antibodies, the antigen to which is considered to be unknown. We postulated that PB antigen is a neo-antigen arising as a result of B cell infection and is related to the benign nature of IM. Paul and Bunnell described PB antibody in 1932 and Downey and McKinley described IM lymphocytes in 1923. Since then the abnormal (Downey) lymphocytes and PB antibody have been considered diagnostic for IM. Using acute phase IM blood, we employed cell separation and identification techniques, to obtain purified or enriched cell populations. We found, in absolute values, a low increase in the B cell population and a high increase of T cells, depending on the lymphocytes/mm3. We were unable to detect PB antigen in IM peripheral blood lymphocytes. EBV (Epstein-Barr virus) believed to cause IM, infects B cells which during maturation develop virus receptor sites and in culture proliferate as established lines. T cells have finite life unless the culture media contains a growth factor. In vivo the Downey cell population consists of 'reactive' T cells, giving rise to the terminology 'self-limiting leukemia' to IM. A double immune system, the PB heterophile and the EBV, exists in IM patients. PB antibodies disappear during convalescence, but PB antigen is found in LL patients. (no Refs)

## 11. IMMUNOLOGIC DIVERSITY OF NODULAR MIXED NON-HODGKIN'S MALIGNANT LYMPHOMA (MEETING ABSTRACT).

**Grogan TM, Hicks MJ, Jolley CS, Jones S, Layton JM**
**Department of Pathology, University of Arizona, Tucson, AZ**

**71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-5, 1982, Boston, Massachusetts. International Academy of Pathology 95 pp., 1982.**

Although differences in the natural history, response to therapy, and survival between nodular poorly differentiated (NPDL) and nodular mixed (NML) lymphomas are described, the precise morphologic distinction between these lymphomas remains uncertain. To determine whether an immunologic distinction between the two exists, 20 nodular lymphomas including 12 NPL and eight NML cases were studied using both frozen section (20 cases) and cell suspension (10 cases) immunofluorescence techniques. The biopsies were stained with immunoglobulin (Ig) light- and heavy-chain reagents and monoclonal antibody to Ia (HLA-DR) antigen using both methods. The E-rosette phenomenon (ESRBC) was examined in suspension alone. All 12 cases of NPDL were monoclonal Ig+, Ia+, and ESRBC-. In contrast, only four of eight NML lymphomas were monoclonal Ig+: three IgM (K) and one IgA (K). The remaining four cases were Ig-, ESRBC- with intense Ia positivity noted. The tissue section method identified the Ia+ cells as especially prominent in the neoplastic nodules. The Ig-, Ia+, ESRBC- phenotype is comparable to the phenotype we have observed in some cases of large cell lymphoma. Our findings indicate that NML has two basic immunologic phenotypes: the monoclonal Ig+ type (similar to NPDL) and the Ig-, Ia+ type (similar to some large cell lymphomas). Since follicular center B cells are Ia+, this does not alter the view that NML is of follicular center origin. (no Refs)

## 12. CELL SURFACE PHENOTYPE AND FUNCTIONAL CHARACTERIZATION OF NON-HODGKIN'S LYMPHOMAS (MEETING ABSTRACT).

**Ford RJ, Davis F, Kusyk C, Lachman LB, Morgan J, Maizel AL**
**University of Texas, M.D. Anderson Hospital, Houston, TX, 77030**

**Proc Am Assoc Cancer Res; 23:993 1982**

The cell surface phenotype of a spectrum of non-Hodgkin's lymphomas (NHL), obtained from untreated patients at the time of lymph node biopsy or splenectomy, was performed using conventional immunologic markers, and a repertoire of T and B cell monoclonal antibodies. In addition, the lymphoma cells were also karyotyped, G-banded, and assayed for a tumor associated nucleolar antigen by immunofluorescence with a heteroantisera. The combination of these parameters were then used to characterize the phenotype of both T and B cell type NHL. Results of these studies indicated a considerable heterogeneity among the subtypes of NHL which may be of clinical significance. To study functional characteristics of the lymphoma cells were assayed for proliferation and differentiation using either mitogens or greatly purified human Interleukin (IL-1 and IL-2) preparations. These studies indicated that purified lymphoma cells could be stimulated in many instances, to proliferate in vitro with the Interleukin preparations. In some cases, differentiation into immunoglobulin-secreting cells was also observed. These studies suggest that many of the lymphoma cells are sensitive to normal immunoregulatory molecules. The combination of cell surface phenotyping correlated with cytogenetics and functional parameters should lead to a better immunopathological characterization of human NHL cells in the near future. (no Refs)

### 13. CHARACTERIZATION OF A HUMAN IL-2 PRODUCING T LYMPHOMA (JURKAT) AND VARIANTS DEFICIENT IN HPRT (MEETING ABSTRACT).

Lakow E, Altman A, Carson DA
Scripps Clinic, La Jolla, CA, 92037
Fed Proc; 41(3):598 1982

IL-2 (Interleukin 2 ) is essential for T cell proliferation and function. Gillis and Watson described a human T cell lymphoma, Jurkat, that secretes IL-2 in vitro after stimulation with phytohemagglutinin (PHA). Current experiments were designed to (a) characterize the surface antigen phenotype of these cells, (b) define optimal conditions for IL-2 secretion, and (c) select and characterize variants deficient in hypoxanthine phosphoribosyltransferase (HPRT) suitable for human T-T hybridization. A mycoplasma-free clone of Jurkat maintained a helper T cell phenotype during continuous growth in our laboratory for six months, binding monoclonal antibodies againt Leu 3a and OKT3 antigens, but not against Leu 2a and Ia antigens. Following stimulation with 1% PHA, Jurkat secrets IL-2 into the medium over a 48 hour period, as measured by 3H-thymidine uptake by a murine IL-2 dependent cell line. Normal peripheral blood T lymphocytes and Jurkat cells produce equivalent amounts of IL-2. Mutants which are deficient in HPRT were selected and cloned by limiting dilution. These mutants secrete IL-2 in amounts equivalent to the parental line. In preliminary experiments, HPRT deficient Jurkat cells have yielded somatic cell hybrids after fusion with normal T lymphocytes. Because HPRT deficient Jurkat cells have a helper phenotype, and clone efficiently, they are ideal for the production of functional human T-T hybridomas. (no Refs)

## DETECTION AND CHARACTERIZATION OF IMMUNE CELL SURFACE MARKERS

### 14. INTERACTIONS OF C-REACTIVE PROTEIN WITH LYMPHOID CELLS.

James K, Baum LL, Vetter ML, Gewurz H
Dept. Immunology/Microbiology, Rush Medical Coll., Chicago, IL, 60612
Ann NY Acad Sci; 389:274-285 1982

The interactions between CRP and peripheral blood lymphocytes were investigated. CRP, in the presence of an appropriate ligand, bound saturably to a small percentage of normal PBL. The characteristics and optimal conditions for this binding were defined using several different assay systems. CRP was found to bind preferentially to cells with the IgG FcR. Binding was increased in the presence of acute phase sera, and higher numbers of cells binding CRP were observed in acute phase individuals. CRP and CRP-CPS had minimal effects upon lymphocyte responsiveness in vitro, although enhancing effects on MLC and CMC reactions, and a slight blastogenic effect, were observed. CRP antigenicity was detected on a small percentage of PBL, and treatment of PBL with anti-CRP and complement led to loss of NK reactivity, suggesting a possible association of CRP with this function. The functional expression of binding of CRP complexes, the relationship of the CRP-binding site to surface CRP antigenicity and the FcR, and the role of these factors in lymphocyte functions such as NK reactivity and recognition, are yet to be determined. (Author abstract) (26 Refs)

### 15. IN VITRO CHARACTERIZATION OF THE ADJUVANT ACTIVITY OF LIPOSOMES CONTAINING HUMAN TUMOR ANTIGENS (MEETING ABSTRACT).

Raphael L, Liu JS, Tom BH
University of Texas Medical School, Houston, TX, 77030
Fed Proc; 41(3):416 1982

Liposomes prepared with LS174T human colon tumor cell membranes stimulated the primary in vitro generation of cytotoxic BALB/c splenocytes (SPC). The kinetics of the induction of SPC was similar for both whole LS174T cells and liposome antigen (MLV-Ag). Specificity of the primed SPC was demonstrated on a variety of human tumor cells. Cold target inhibition results revealed 72% of the cytotoxic activity directed at tumor and not HLA antigens. Elimination of Thy 1.2+ cells abolished the lytic activity of the immune cells indicating T cell involvement. Addition of Thymocyte-conditioned media improved the ability of antigens to elicit effector cells. The adjuvant effect of MLV-Ag is mediated primarily by tumor antigens exposed on the outer surface of liposomes. Trypsinization of the MLV-Ag which eliminated 96% of the surface protein reduced the ability of the MLV-Ag to induce cytotoxic SPC. Dose response of MLV-Ag showed that while 10ug was the threshold, 100ug protein induced maximal responses. Since only 50% of the Ag is exposed on the MLV-Ag surface a critical Ag density of 50ug is necessary for the induction of cell-mediated immunity. Parallel studies with breast tumor Ag have now been shown to generate specific cytotoxic cells. Ag have now been shown to generate specific cytotoxic cells. Thus, MLV-Ag may provide a means to investigate cell-Ag conditions necessary for inducing cytotoxic T cells, as well as a potential system for selecting desired immune responses. (no Refs)

### 16. CYTOTOXICITY OF NATURAL KILLER CELLS. CORRELATION WITH EMPERIPOLESIS AND SURFACE ENZYMES.

Burns ER, Zucker-Franklin D, Valentine F
(c/o Zucker-Franklin), New York Univ. Medical Center UH 455, 550 First Ave., New York, NY, 10016
Lab Invest; 47(1):99-107 1982

Cell-mediated cytotoxicity involving natural killer cells requires contact between effector and target cells for effective cytolysis. Ultrastructural studies of biopsies of primary human malignant melanoma showed mononuclear leukocytes to be located in close proximity to tumor cells and, on occasion, within the confines of the melanoma cell itself. This phenomenon, called emperipolesis, was examined in vitro to determine whether the same population of cells that exhibits emperipolesis is responsible for cytotoxicity. Since natural killer cells have been identified morphologically and functionally as large granular lymphocytes with surface receptors for the Fc portion of immunoglobulin (FcR+ cells), lymphocytes were depleted of FcR+ cells, and their cytotoxicity and ability to emperipolese were measured. Both of these properties were markedly diminished (88 and 85%, respectively). Systematic comparison of emperipolesis and cytotoxicity from donors known to exhibit either high or low lymphocyte cytotoxicity showed perfect concordance. Ultrastructural analysis of in vitro emperipolesis revealed the emperipolesing lymphocytes to be FcR+ cells establishing identity with the large granular cells known to mediate cytotoxicity. The morphologic marker found in both FcR+ cells, purified by rosetting techniques, and in emperipolesed lymphocytes consisted of cytoplasmic parallel tubular arrays. Further studies designed to elucidate a mechanism for cytotoxicity and emperipolesis implicated cell surface proteases

as mediators of these activities. Competitive inhibition of surface proteases with artificial and natural inhibitors markedly reduced both cytotoxicity and emperipolesis. Therefore, it is likely that lymphocytes that are FcR+ participate in cell-mediated cytotoxicity through mechanisms involving cell contact and enzyme-initiated damage of target cells. Emperipolesis represents one type of effector-target cell contact leading to cytotoxicity. (Author abstract) (43 Refs)

### 17. STUDY OF PULMONARY ALVEOLAR MACROPHAGES AND STUDY OF HISTOCHEMICAL MARKERS FOR PULMONARY ALVEOLAR MACROPHAGES AND MACROPHAGES IN BRONCHOGENIC CARCINOMAS (MEETING ABSTRACT).

Soufleris AJ, Pretlow TP, Pretlow TG
University of Alabama in Birmingham, Birmingham, AL, 35294
Fed Proc; 41(3):433 1982

During the course of morphometric studies of stromal cells from human tumors, it became necessary to find markers that would permit the identification of macrophages in tissue sections. Enzyme histochemical methods were applied to 1-2 micron sections of lungs and contiguous bronchogenic carcinomas embedded in plastic. A considerable degree of variability in enzymatic activity was observed among different macrophages and among different patients. The most commonly useful marker for pulmonary alveolar macrophages was alpha-naphthyl butyrate esterase; 50-87% of pulmonary alveolar macrophages showed some evidence of this marker histochemically. Pulmonary alveolar macrophages demonstrated evidence of naphthol AS-D chloroacetate esterase in 41-86%, peroxidase in 3-86%, acid phosphatase in 14-100%, and stainable iron in 0-96% of cells. All of these markers were observed in some stromal cells of bronchogenic carcinomas. The lack of any uniformly demonstrable marker enzyme in pulmonary alveolar macrophages suggests that it will be necessary to recognize several subcategories of stromal cells recognized primarily by their observed phenotypic expressions of histochemical markers. (no Refs)

## LYMPHOCYTE AND DIFFERENTIATION ANTIGENS

### 18. MONOCLONAL ANTIBODIES AGAINST B-CELL DIFFERENTIATION ANTIGENS CHARACTERIZE VARIOUS FORMS OF CHRONIC LYMPHATIC LEUKEMIA.

Muller C, Wernet P, Ziegler A, Heinrichs H, Steinke B, Waller HD
Abt. II, Med. Klinik Tubingen, Tubingen, W. Germany
Verh Dtsch Ges Inn Med; (87):748-750 1981

The degree of differentiation of B-cells from 13 patients with chronic lymphocytic leukemia (CLL) and 2 patients with immunocytoma (IC) was studied using selected monoclonal antibodies. Peripheral WBC counts were 7,900-240,000/cubic mm. The diagnosis of CLL was confirmed in nine patients by lymphocytic infiltration of the bone marrow and peripheral lymphocytosis; in six patients the diagnosis was also confirmed histologically. Lymphocytes were isolated from heparinized blood; surface antigens were identified by indirect immunofluorescence assays. Test antibodies were directed against human lymphocytic antigens (HLA) A, B, and C, HLA-D, various T-cell subpopulations, and B-cells. In all the patients studied, 80-90% of lymphocytes were classified as B-cells, as indicated by surface immunoglobulins and expression of HLA-DR antigens. Twelve patients showed expression of IgM on cell surfaces; 6 of these also showed IgD. Approx 5-10% of the cells were classified as residual T-cell populations. All B-cells reacted with antibodies that also reacted with some T-cells. B-cells also reacted with antibodies that reacted with some normal B-cell populations. Results indicate that B-cells from patients with CLL are derived from an early stage of B-cell differentiation, and that these cells consist of various distinct subpopulations. (9 Refs) (In GER)

### 19. THE EXPRESSION OF THY-1 ANTIGEN ON HUMAN LYMPHOID CELLS (MEETING ABSTRACT).

Saji F, Negoro T, Tanigaki N
Department of Molecular Immunology, Roswell Park Memorial Institute, Buffalo, NY, 14263
Fed Proc; 41(3):795 1982

Whether or not the human homologue of murine Thy-1 antigen is expressed on lymphoid cells has been a controversial issue. Our present study using antiserum specific for human Thy-1 antigen indicates that peripheral blood lymphocytes (cultured or uncultured) and cultured T-cell leukemia cells differ distinctly in the expression of Thy-1 antigen: both carry Thy-1 antigen, but the former do not expose it on the cell surface while the latter do. The rabbit antiserum was raised against a preparation of human Thy-1 antigen purified from cells of a human T-cell leukemia cell line, SKW-3. It showed a clear binding with cells of T-cell lukemia cell lines by membrane immunofluorescence and in the cellular binding assay, both of which detect the antigens exposed on cell surface. Peripheral blood lymphocytes were totally negative by both immunofluorescence and the cytotoxicity assay. On the other hand, both cultured T-cell leukemia cells and peripheral blood lymphocytes gave a positive reaction in a binding inhibition assay which uses detergent-solubilized specimens and thus detects both exposed and hidden antigens. Analysis of the subcellular distribution of Thy-1 antigen on peripheral blood lymphocytes revealed that its localization is restricted to cell membranes. (no Refs)

### 20. IDENTIFICATION OF THE T CELL SUBSET THAT PRODUCES HUMAN GAMMA INTERFERON (GAMMA-IFN) (MEETING ABSTRACT).

Ozer H, Grossmayer B, Nussbaum-Blumenson A, Sheedy D, O'Malley J
Roswell Park Memorial Institute, Buffalo, NY, 14263
Proc Am Assoc Cancer Res; 23:965 1982

Positive and negative selection procedures as well as cytofluorographic analysis and lysis with monoclonal antibodies were utilized to identify the T cell subset that produces human gamma-IFN. Lymphocytes were separated on the basis of their Fc receptors for IgG and IgM and their reactivity with the monoclonal antibodies OKT3, OKT4, OKT8, OKT11a and OKM1. Isolated T cell subsets were incubated with the gamma-IFN inducer, PHA (phytohemagglutinin). On days 3 and 6 the cell supernatants were harvested, assayed for interferon activity and characterized for pH and heat lability, as well as reactivity with anti-alphaIFN antibody. The lymphocyte subset producing gamma-IFN was shown to be E+, Fcgamma+, OKM1+ and OKT11a but OKT3-, OKT4-and OKT8-. Gamma-IFN production by this subset was resistant to doses of x-irradiation which abrogated miotogen-induced T suppressor function but was highly sensitive to low doses of 4-

hydroperoxycyclophosphamide. These data demonstrate that gamma-IFN is produced, or possibly regulated, by the Fcgamma+, OKM1, OKTIIa+ T subset. The antiproliferative activity of gamma-IFN may be responsible for the previously described suppressor function of these T cells and may distinguish this subset from the suppressor/cytotoxic functions of the OKT8+ subset. (no Refs)

## 21. A CYTOTOXIC MONOCLONAL ANTIBODY IDENTIFYING AN ANTIGEN PRESENT ON ACTIVATED LYMPHOID CELLS AND TUMORS.

**Teplow DB**
**University of Washington, Seattle, WA**
**Diss Abstr Int [B]; 42(6):2302-B 1981**

Murine cytolytic T lymphocytes (CTL) were injected into semisyngeneic animals. The CTL used were specific for the murine leukemia virus (MuLV)-induced tumor LSTRA. Spleen cells from hyperimmunized animals were fused with NS-1 myeloma cells to produce antibody-secreting hybrids. One hybrid, number 228, produced an antibody capable, in the presence of complement, of abrogating CTL killing in chromium release assays. The species, strain, tissue and cellular distribution of the antigen (Ag 228) defined by this monoclonal antibody were extensively analyzed. Ag 228 is present in large amounts on mitogen-activated T-lymphocytes, syngeneic and allogeneic CTL, mitogen-activated B-lymphocytes and certain leukemias. It is not present at significant levels on resting lymphoid cells, bone marrow cells, testicular cells, fetal cells or a variety of adherent tumor and non-tumor cell lines of human, rat and mouse origin. In vivo data suggest that Ag 228 may play a role, either at the effector cell or target cell level, in the regulation of protective immune responses against tumors. Ag 228 is a non-viral antigen which, in preliminary biochemical studies, appears to be a protein with a molecular weight of approximately 30,000. Its characteristics are similar to those of Ly-19 antigen, non-HLA-DR-related human lymphocyte activation antigens and Ii chains of human, rat and mouse Ia antigens. (no Refs)

## 22. CELL SURFACE ANTIGEN PHENOTYPES AND ENZYME EXPRESSION PATTERNS OF TWO MURINE T-CELL LYMPHOMAS DERIVED FROM EARLY AND/OR MATURE THYMUS CELLS.

**Dullens HF, Hilgers J, Van Basten CD, De Weger RA, De Heer E, Den Otter W**
**Dept. Pathology, State Univ. Utrecht, Pasteurstraat 2, 3511 HX Utrecht, The Netherlands**
**Leuk Res; 6(3):425-428 1982**

Expression of cell surface antigens on SL2 and GRSL13 cells and enzyme cytochemistry of murine SL2 and GRSL13 lymphoma cells were investigated. SL2 lymphoma occurred as a spontaneous tumor in DBA/2 mice, and GRSL13 lymphoma occurred as a spontaneous lymphoma in GRS mice. While T200 antigen expression was high on both lymphomas, Thy1 was low on GRSL13 and high on SL2. Significant difference between the two lymphomas was obtained using antibodies 30-G12 (anti-T200) and 30-H11 (anti-glycolipid) with positivity on GRSL13 and no reaction on SL2; a reverse pattern was seen with antibodies 53-7.3 (anti-Lyt1) and 53-6.7 (anti-Lyt2). Since ThB and the glycolipid detected by antibody 30-H11 were expressed on bone marrow cells and since ThB was not expressed at all on peripheral T cells, the antigens are apparently characteristic for the more primitive cells in the thymic series. Results showed that GRSL13 represents a T cell of a more primitive immature type, while SL2 represents a more mature T cell. Enzymes present and clearly expressed in the lymphomas as well as the majority of thymus cells were acid phosphatase, beta-glucuronidase, non-specific esterase, and alphan-aphthyl-acetate-esterase. No clear difference was observed between the two lymphomas and the normal thymus cells. (17 Refs)

## 23. CROSS-REACTING ANTIGENS ON L5178Y CELLS WHICH SERVE AS TARGETS FOR CYTOTOXIC T-LYMPHOCYTE LYSIS DURING ESTABLISHMENT OF THE TUMOR DORMANT STATE.

**Weinhold KJ, Wheelock EF**
**(c/o Wheelock) Dept. Pathology and Lab. Medicine, Hahnemann Medical Coll., Philadelphia, PA, 19102**
**Cancer Res; 42(9):3607-3616 1982**

We have attempted to identify the antigen on L5178Y cells that is the target for peritoneal cytotoxic T-lymphocytes (CTL) generated in L5178Y-O (original) immunized and challenged DBA/2 mice during establishment of the L5178Y cell tumor dormant state. These CTL exhibited in vitro lytic activity against methylcholanthrene-induced L5178Y and P815Y cells as well as Gross virus-induced BALB/c cells but not against a variety of other H-2d-tumor cell lines. The pattern of susceptibility to cell-mediated immune cytolysis was identical to the pattern of AB-dependent complement-mediated cytolysis produced by a rabbit anti-L5178Y antiserum. Quantitative expression of surface H-2d determinants was not a limiting factor in tumor cell lysis by CTL. The degree of CTL lysis of the susceptible cell lines was directly related to the amount of tumor-associated antigen expressed on the cell surface. The pattern of in vitro susceptibility to CTL lysis correlated well with in vivo transplantation resistance. The L5178Y cell antigen target for both CTL and Ra-anti-L5178Y serum lysis is likely to be either an endogenous AKR ecotropic viral glycoprotein with a mol wt of 71,000 or one of two cell surface determinants, at Mr 85,000 and 135,000. These higher-mol-wt antigens are neither endogenous AKR ecotropic viral-induced nor murine leukemia virus group-specific precursor structural proteins but may be transformation antigens shared by the susceptible tumor cell lines. (Author abstract) (37 Refs)

## 24. INFLUENCE OF B LOCUS ON AVIAN VIRAL INDUCED TUMORS.

**Cauchy L, Dambrine G, Coudert F**
**Station de Pathologie aviaire et de Parasitologie, I.N.R.A., Centre de Recherches de Tours-Nouzilly, F-37380 Monnaie, France**
**Bull Cancer (Paris); 69(2):194-198 1982**

Since early in the century Avian Cancers were described as induced by viruses which later were known of DNA and RNA types. The susceptibility of birds was found different according to the genetic lines of the chickens and specially to the B locus blood group. since the B locus of birds was strongly associated with the Major Histocompatibility Complex (MHC) it was of interest to review the last reports on the influence of the B locus on viral induced tumors. In Marek's Disease due to a DNA virus (Herpes type) the B21 allele expresses the greater resistance compared with other B alleles although non-B factors could be involved as demonstrated with the lymphocyte factor Ly-4. The possible mechanisms of the influence of B locus on the resistance against Marek's Disease are discussed. The tumors induced by RNA viruses (Avian Leucosis Sarcomas) develop or regress following genetic characters closely related to MHC. Differences of resistance exist between B alleles. Complementary genes should be present to fully express

the resistance. The relationship between MHC-B locus and resistance to tumors stimulates the actual assays. Since a number of parameters remain still unknown further research should be done in order to evidence the involved mechanisms of the resistance. (Author abstract) (26 Refs) (In FRE)

### 25. LECTIN-BINDING CHARACTERISTICS OF HUMAN NATURAL KILLER CELLS.

Vose BM, Blackledge G, Crowther D, Gallaher J
Dept. Immunology, Paterson Lab., Christie Hosp. and Holt Radium Inst., Manchester M20 9BX, England
Immunology; 46(3):619-627 1982

Human natural killer (NK) cells separated initially by density centrifugation of lymphocytes (E+) forming rosettes with sheep red blood cells (SRBC), were further fractionated on gradients of bovine serum albumin (BSA). Low density fractions contained effector cells which displayed high cytotoxicity against the NK-sensitive erythroleukemic cell line, K562. These low density cells, which expressed receptors for Fc and the monoclonal antibody OKM1, showed enhanced cytotoxicity when treated with lymphoblastoid interferon (IFN-alpha). They also showed an increased response to phytomitogen in comparison with unseparated cells or those recovered from high density fractions. Two lymphocyte subsets one of high and one of low lectin binding capacity were identified in the E+ populations by their reactivity with Lens culinaris agglutinin (LCA). High LCA binding was observed only in low density fractions and was associated with a marked enrichment of NK activity. This property was used to separate the NK active population in E+ cells by fluorescence-activated cell sorting (FACS). These data add a new dimension to the cell surface properties of human NK cells and suggest the presence of LCA-reactive glycoproteins which are either enriched in, or uniquely associated with, cells of the NK subset. The experiments indicate that lectins can serve as useful probes of lymphocyte function and provide the basis for effective cell sorting. (Author abstract) (26 Refs)

### 26. A CLONED CELL WITH NK FUNCTION RESEMBLES BASOPHILS BY ULTRASTRUCTURE AND EXPRESSES IGE RECEPTORS.

Galli SJ, Dvorak AM, Ishizaka T, Nabel G, Simonian HD, Cantor H, Dvorak HF
Dept. Pathology, Beth Israel Hosp., Boston, MA, 02215
Nature; 298(5871):288-290 1982

Cloned mouse cell line Ly1-2-NK-1+/11 was studied morphologically and evaluated whether it shared other properties of basophilic leukocytes. Analysis by direct binding of 125I-labeled monoclonal mouse IgE demonstrated that it expressed high-affinity plasma membrane receptors (FcepsilonR) specific for IgE antibody. The binding of 125I-IgE was specific: it was inhibited by unlabeled mouse IgE but neither by normal mouse IgG nor by rabbit IgG, even in 133-fold molar excess. Findings indicated that cells sharing morphological and biochemical features of basophilic granulocytes can mediate natural killer lysis. (37 Refs)

## CHANGES IN SURFACE MARKERS ASSOCIATED WITH IMMUNE CELL MATURATION AND ACTIVATION

### 27. ANTITUMOR ACTIVITY AND HYDROGEN PEROXIDE RELEASE BY MACROPHAGES ELICITED BY TREHALOSE DIESTERS.

Lepoivre M, Tenu JP, Lemaire G, Petit JF
Institut de Biochimie, Batiment 432, Universite de Paris-Sud, 91405 Orsay, France
J Immunol; 129(2):860-866 1982

Trehalose diesters (natural 6,6'-trehalose dimycolate from Mycobacterium tuberculosis or synthetic (a 76 carbon atom analogue)), when suspended in water, given stable and well-defined emulsions. These emulsions, injected ip in mice significantly limit the growth of P815 syngeneic mastocytoma cells. They elicit macrophages with a cytostatic activity against P815 cells in vitro, strong enough to be expressed at low effector to target ratios (E/T = 1.4) or after a short coincubation period (2 hr). The antitumor potential of these macrophages seems to coincide with their ability to release H2O2 upon pharmacologic triggering. Depressed levels of alkaline phosphodiesterase and beta-galactosidase are proposed as other biochemical markers of cytostatic macrophages. (Author abstract) (44 Refs)

### 28. HUMAN MONOCYTE (MO) - MACROPHAGE (M) ACTIVATION AND PROLIFERATION IN RESPONSE TO HUMAN EFFUSION FLUIDS (HEF) (MEETING ABSTRACT).

Polesz B, Zamkoff K, Ruscetti F, Mier J, Davey F, Rudolph A, Ginsberg S, Comis R
Veterans Administration Medical Center, Syracuse, NY, 13210
Proc Am Assoc Cancer Res; 23:1035 1982

We studied the effect of HEF on HEF-derived M and on heterologous peripheral blood MO (PBMO). Sterile HEF exudates were centrifuged and the supernatants treated at 56 degrees for 45 min. Both M and PBMO demonstrated marked evidence of activation in response to HEF compared with controls with increased cell size, cytoplasmic granules, vacuole formation, giant cell formation, phagocytic and lysozyme activity. Cells grew as monolayers with morphology, staining pattern, cell surface markers, and functional properties consistent with MO and M. The activation factors(s) in HEF precipitates in 75% NH4SO4, is non-dialyzable, doesn't filter through a 10,000 MW Amicon membrane and chromatographs at 25,000 on Ultragel ACA54. Both crude and chromatographed HEF were negative for colony stimulating activity (CSA) for human and mouse bone marrow. Continuous culture of M from 15 separate HEF was achieved. Two cell lines (MAC 1 and 2) are now independent of HEF, have been cultured greater than 2 yrs, have hyperdiploid human karyotypes, and elaborate CSA upon treatment with indocin. Active HEF also induced PBMO proliferation, measured by H3-thymidine incorporation and cell counts. PBMO growth was not as marked as that of M, and early studies indicate that it is dependent upon conditioning of the culture media by the PBMO. CSA activity in HEF + PBMO conditioned media was greater than HEF-cultures. (no Refs)

## 29. ACID HYDROLASES AS MARKERS OF MATURATION IN B-CELL CHRONIC LYMPHOCYTIC LEUKEMIA.

Grossi CE, Zicca A, Leprini A, Cadoni A, Pistoia V, Ferrarini M
Instituto di Anatomia Umana Normale della Universita, Via De Toni, 14, 16132, Genova, Italy
Blood; 60(1):220-227 1982

Malignant lymphocytes from 30 B-cell chronic lymphocytic leukemia (B-CLL) patients were studied for the cytochemical localization of two acid hydrolases, alpha-naphthyl acetate esterase (ANAE) and acid phosphatase (AT). The large majority of the cells stained for both ANAE and AP in 7 cases, for AP only in 18 cases, and were negative for both the enzymes in 5 cases. Ultrastructural analysis revealed that the cells that displayed more mature morphological features, such as well developed smooth and rough membrane compartments, were those positive for acid hydrolases. The ANAE and AP are expressed by B cells at late stage of maturation was confirmed by the finding that some lymphocytes and all of the plasmacytoid lymphocytes and plasma cells from Walderstrom's macroglobulinemia, from mixed cryoglobulinemia, and from multiple myeloma patients stained strongly for both ANAE and AP. Using the expression of acid hydrolases and certain ultrastructural features as markers of cell differentiation, it was possible to demonstrate a process of maturation within the single B-CLL clones with accumulation of the cells at stages that differed in the various cases. (Author abstract) (37 Refs)

## 30. A B-LYMPHOCYTE-SPECIFIC HIGH-TURNOVER PROTEIN: CONSTITUTIVE EXPRESSION IN RESTING B CELLS AND INDUCTION OF SYNTHESIS IN PROLIFERATING CELLS.

Rahmsdorf HJ, Mallick U, Ponta H, Herrlich P
Kernforschungszentrum Karlsruhe, Universitat Karlsruhe, Postfach 3640, D-7500 Karlsruhe 1, W. Germany
Cell; 29(2):459-468 1982

A basic B-cell-specific protein of 35,000 daltons (XM1) is expressed at a high rate - comparable to actin - in resting splenic B lymphocytes of various species. Splenic or thymic T cells or fibroblasts do not express this protein. Upon polyclonal stimulation of B lymphocytes or in proliferating B-lymphocyte-derived cell lines, the synthesis of XM1 is switched off, but it is reinduced by agents that arrest replication, such as mitomycin C, hydroxyurea, ultraviolet light or gamma irradiation. Induction of XM1 after mutagen treatment is fast; the synthesis is regulated on the level of transcription of RNA processing. XM1 is turned over with half-life of less than 2 hr. XM1 is glycosylated. From compartment analysis and Triton solubilization it appears that XM1 is bound to the nuclear membrane. (Author abstract) (60 Refs)

## 31. TOTAL AND SURFACE-LOCATED SIALIC ACID LEVELS IN NORMAL AND LEUKEMIC LYMPHOCYTES: RELATIONSHIP TO T AND B CELL NATURE AND TO LOCATION IN VIVO.

O'Kennedy R, Smyth H, Corrigan A, Clynes M
Sch. Biological Sciences, Natl. Inst. Higher Education, Dublin 9, Ireland
Eur J Cancer Clin Oncol; 18(5):437-446 1982

Unfractionated normal blood lymphocytes (predominantly T lymphocytes) showed significantly elevated total and neuraminidase-susceptible sialic acid compared with CLL lymphocytes (predominantly B lymphocytes). T-enriched fractions from normal blood contained about three-fold the sialic acid content of the corresponding T-depleted fractions, and similarly low values were also obtained for T-depleted fractions from tonsils. Thus the reduced sialic acid levels in CLL lymphocytes appear to be due to their B cell nature. In contrast to the situation in normal peripheral venous blood, tonsillar T and B cells did not differ markedly in sialic acid content, suggesting that for T cells maturity and/or location in vivo are important determinants of this parameter. Results with calf thymocytes were in agreement with this. Sialic acid was estimated in malignant B and T lymphoblasts. Shedding of sialic acid-containing moieties from lymphocytes was also examined. (Author abstract) (50 Refs)

## 32. MURINE B LYMPHOMAS: MODELS FOR IMMUNOGLOBIN EXPRESSION IN B CELL DEVELOPMENT.

Word CJ
University of Virginia, Charlottesville, VA
Diss Abstr Int [B]; 42(9):3582-B 1982

Individual clones of three B lymphoma cell lines (A20-1.11, X16C-4.3, K46-056) were found to synthesize two intracellular species of gamma 2a heavy chain which differ in apparent size by approx 6,000 daltons. The smaller gamma 2a heavy chain species is secreted by the cell and the larger gamma 2a heavy chain species is localized on the external cell membrane. Two species of mRNA, which apparently encode the two gamma 2a heavy chain species, were detected in the cytoplasm of the cells. It appears that the smaller (2.0 kb) mRNA species codes for the secreted gamma 2a heavy chain and the larger mRNA species (4.0 kb) codes for the membrane gamma 2a heavy chain. Fusion of the A20-1.11 or X16C-4.3 B lymphoma to myeloma cell lines results in hybrids expressing the more differentiated myeloma phenotype. That is, the expression of the secreted form of the lymphoma gamma 2a heavy chain is amplified as much as 150 fold while the expression of the membrane form of the lymphoma gamma 2a heavy chain polypeptide and corresponding mRNA is greatly diminished or abolished in the hybrid. Less than five percent of normal B lymphoid cells or plasma cell tumors express lambda light chains, and only rare tumors have been described that simultaneously express both lambda and kappa light chains in a single cell. However, three cloned B lymphoma cell lines (K46-056, B17-1.11, X16C-4.3) were found to express both lambda and kappa light chains. Different patterns of assembly of the light chains to the heavy chains were found. (no Refs)

## 33. THE ROLE OF INTERFERON IN THE MAINTENANCE OF NATURAL KILLING BY HUMAN T LYMPHOCYTE SUBSETS (MEETING ABSTRACT).

Peterman GM, Klimpel GR, Stanton GJ, Altman LC
University of Washington, Seattle, WA, 98195
Fed Proc; 41(3):801 1982

We have previously reported that freshly isolated human T lymphocyte subsets differ in their ability to kill K562 tumor cells in assays of natural killing and that these cells maintain their cytolytic capacity when stimulated in mixed lymphocyte culture (MLC). In order to assess the role of interferon (IFN) in K562 cytolysis, we examined IFN levels in supernatants from MLC stimulated T cell subsets and the role of exogenous IFN in the maintenance of K562 killing. IFN levels were measured by viral plaque reduction. T cells were isolated by srbc rosette formation and Ficoll-Hypaque centrifugation. T cells which lost the ability to form srbc rosettes after incubation in 5mM theophylline (T-sens cells) and T cells which retained this ability (T-res cells) produced equivalent levels of IFN

when stimulated in MLC. The IFN produced by these T cell populations was completely neutralized by antisera against IFN gamma while antibodies directed against IFN alpha and IFN beta had no effect. In contrast, T cells cultured alone failed to produce IFN and did not kill K562. Addition of partially purified IFN gamma (10(5) U/mg protein) to cultured T cell subsets markedly enhanced their ability to kill K562. These results suggest that maintenance of K562 cytolysis by MLC stimulated T cells is mediated by the production of IFN gamma. (no Refs)

### 34. TRANSMEMBRANE POTENTIAL CHANGE (TPC) OF SENSITIZED HUMAN LEUKOCYTES BINDING ORGAN-SPECIFIC CANCER NEOANTIGENS (OSN) (MEETING ABSTRACT).

**Shenouda G, Thomson DM**
**The Montreal General Hospital Research Institute, Montreal H2G 1A4, Canada**
**Fed Proc; 41(3):311 1982**

In this study we measured the TPC of leukocytes before and after exposure to extracts of the sensitizing or control cancer. The TPC was measured by the uptake of the permeant lipophilic cation [3H-Phenyl]Tetraphenylphosphonium bromide which equilibrates rapidly across biological membranes and the measurement of its distribution reflects the magnitude and direction of TPC. Leukocytes from early breast cancer patients when challenged with the breast OSN showed TPC. Leukocytes from patients with advanced breast cancer showed no TPC when challenged with breast OSN, unless the leukocytes were exposed before to PGE2 5 x 10(-6) M. The TPC was immunologically specific. The mechanism of the TPC was characterized. Monocytes armed with cytophilic antitumor antibody showed TPC when challenged with the sensitizing OSN, whereas T-lymphocytes did not. The TPC of leukocytes consisted of 2 reactions. There is TPC of the armed monocytes when they bind the OSN that occurred in the presence of ETYA or FPL 55712; and there is TPC induced in bystander cells by leukotrienes released from the monocytes when they bind OSN that could be blocked by ETYA or FPL 55712. TPC is an early event in stimulus-response coupling of human leukocytes reacting with their sensitizing cancer extracts. (no Refs)

### 35. INHIBITION OF CONCANAVALIN A RESPONSE DURING OSTEOPETROSIS VIRUS INFECTION.

**Price JA, Smith RE**
**(c/o Smith) Dept. Microbiology and Immunology, Duke Univ. Medical Center, Box 3020, Durham, NC**
**Cancer Res; 42(9):3617-3624 1982**

Infection of animals with oncogenic viruses frequently leads to an immunosuppressed state. We have examined immunosuppression induced by an avian osteopetrosis virus, myeloblastosis-associated virus of subgroup B inducing osteopetrosis [MAV-2(O)], and our results suggest that this virus induces immunosuppression by a novel mechanism. Lymphoid cells from osteopetrotic chickens did not respond to a wide dose range of concanavalin A (Con A) over a wide cell density range. Failure to undergo blastogenesis was not due to a lack of Con A-binding sites, since 125I-labeled Con A bound to lymphocytes from infected and uninfected chickens. Infected lymphocytes failed to respond to uninfected chickens. Infected lymphocytes failed to respond to sodium metaperiodate stimulation, indicating that failure of blastogenesis was not due to a blockage of Con A receptor sites. MAV-2(O) infection of chicks 8 days of age resulted in a transient immunosuppression which appeared 1 to 2 wk after infection. Cell-mixing experiments showed that MAV-2(O)-induced immunosuppression was not attributable to suppressor cells. In contrast, adherent cells from normal lymphoid preparations restored mitogenicity to lymphocytes from MAV-2(O)-infected animals. Adherent cells were present in the spleen and peripheral blood lymphocytes of MAV-2(O)-infected chickens in numbers comparable to those of the uninfected animal, and both sets of cells contained Fc-dependent phagocytic activity and nonspecific esterase. Peritoneal exudate cells were elicited from osteopetrotic and normal chickens in similar numbers. We conclude that MAV-2(O) induces immunosuppression by interfering with an accessory function of macrophage-like adherent cells. (Author abstract) (55 Refs)

### 36. EXPRESSION OF XENOTROPIC MURINE LEUKEMIA VIRUSES.

**Morse HC, Hartley JW**
**Lab. Microbial Immunity, Natl. Inst. Allergy and Infectious Diseases, Bethesda, MD, 20014**
**Curr Top Microbiol Immunol; 98:17-26 1982**

Expression of xenotropic murine leukemia viruses (X-MuLV) and X-MuLV-encoded glycoprotein 70 (gp70) antigens was studied in various strains of mice. Genetic information from X-MuLV was found in all strains of mice; expression of this information as infectious virus or gp70 antigens was negatively controlled in most strains. In strains that express high levels of infectious MuLV, negative control was overcome in a variety of ways. Expression of infectious MuLV was not related to the strain of mouse. Expression of MuLV as infectious virus or X-MuLV-coded cell surface antigens (XenCSA) was determined by different factors. In most inbred strains of mice levels of XenCSA were controlled by genes that govern differentiation of T-lymphocytes. Expression of X-MuLV information in T-cells was not related to expression in B-cells. Crosses between inbred strains show different forms of genetic control of the expression of X-MuLV. Findings show no evidence that the products of X-MuLV genes play a role in any normal physiological process. Such a role is, however, not excluded by the evidence. (29 Refs)

## EFFECTS OF CHEMICAL AND PHYSICAL AGENTS ON IMMUNE SURFACE MARKERS

### 37. EFFECT OF ACYCLOVIR ON VARIOUS MURINE IN VIVO AND IN VITRO IMMUNOLOGIC ASSAY SYSTEMS.

**Quinn RP, Wolberg G, Medzihradsky J, Elion GB**
**Wellcome Res. Lab., 3030 Cornwallis Road, Research Triangle Park, NC, 27709**
**Am J Med; 73(1A):62-66 1982**

In two in vitro tests, lymphocyte-mediated cytotoxicity and neutrophil chemotaxis, acyclovir showed no inhibitory effects at concentrations as high as 600 uM. The compound inhibited rosette formation with nonimmune mouse lymphocytes in vitro by approximately 50% at 15.8 uM. The significance of this inhibition is unclear. In four in vivo tests in mice which measured humoral and cell-mediated immunity (complement-dependent cellular cytotoxicity, complement-independent cellular cytotoxicity, delayed hypersensitivity and graft vs host reaction) acyclovir showed no inhibitory effects at single doses up to 200 mg/kg given on Day 2 after antigenic stimulation. Four daily doses of acyclovir at 50 mg/kg per day had no effect on the numbers of hemolytic IgM antibody-forming cells in the

spleen when assayed on Day 4. At the higher dosage of 100 mg/kg per day for 4 days, there was a slight reduction in the numbers of these cells. There was no significant decrease in hemagglutinin or hemolysin antibody titers after four daily doses of acyclovir up to 200 mg/kg. (Author abstract) (16 Refs)

## 38. EFFECT OF ADOPTIVE IMMUNOTHERAPY USING BONE MARROW TRANSPLANTATION AND THYMOSTIMULIN ON IMMUNITY IN CANCER PATIENTS.

Grinevich IuA, Kamenets LIa, Ganul VL, Okulov LV, Kogut GI, Glukhen'kaia GT
Res. Roentgenoradiological and Oncological Inst., Kiev, USSR
Klin Khir; (5):33-36 1982

The efficacy of adoptive immunotherapy was evaluated in 40 patients with Stage III esophageal cancer and in 142 with cancer of the proximal region of the stomach. The patients received preoperative radiotherapy (500 rads/day, total dose 2,500-3,000 rads) and surgery. Within 2-3 wk after the surgery, the patients received transplantation of autologous bone marrow preincubated with thymostimulin. The preoperative therapy and surgery resulted in a marked decrease in lymphocyte count. The bone marrow transplantation did not affect the count of rosette-forming cells or the index of lymphocyte migration in the presence of autologous plasma; it did, however, enhance production of IgA and IgG. Transplantation of bone marrow preincubated with thymostimulin brought about more effective normalization of the indices of cellular and humoral immunity than transplantation of bone marrow that was not preincubated with the thymostimulin. (12 Refs) (In RUS)

## 39. A PHORBOL ESTER TUMOR PROMOTER INDUCES CHANGES IN THE EXPRESSION OF IMMUNOGLOBULINS AND DR ANTIGENS IN HUMAN LYMPHOBLASTOID CELLS.

Roth P, Halper JP, Weinstein IB, Pernis B
(c/o Pernis) 1218 Health Sciences Center, Dept. Microbiology, Columbia Coll. Physicians and Surgeons, 701 W. 168th St., New York, NY, 10032
J Immunol; 129(2):539-544 1982

The present study indicates that 12-O-tetradecanoyl phorbol 13-acetate (TPA) can induce either increases or decreases in the relative expression of membrane-associated IgM and IgD as well as the expression of other markers of lymphocyte differentiation on human B lymphoblasts, depending on the clone studied. The changes in membrane Ig expression are apparent within 24 hr and are maximal at about 48 hr after the addition of the compound. In clone BL, TPA decreases the membrane IgM/IgD ratio as determined by the percentage of cells bearing these isotypes and by their densities on single cells. In clone MW-E, TPA has the opposite effect. Although these changes are followed by an increase in Ig secretion by MW-E cells, measured by immunofluorescence and the protein A plaque assay, There is no induction of Ig secretion in BL cells. In addition, TPA increases the expression in BL of an additional B lymphocyte marker, the D region-related (DR) antigens, while having the opposite effect in MW-E. In two sublines of Daudi, a membrane IgM-positive, IgD-negative, nonsecreting cell line, TPA treatment resulted in the expression of membrane IgD without the induction of Ig secretion. Thus, the TPA-induced changes in the IgM/IgD ratio and Dr antigen expression are inversely related and are not due to differential proliferation of subpopulations. Taken together, it appears that, depending on the particular clone of B lymphoblasts studied, TPA can induce or inhibit a coherent program of B lymphocyte maturation. (Author abstract) (52 Refs)

## 40. SELECTIVE EFFECTS OF ADRIAMYCIN IN MURINE HOST DEFENSE SYSTEMS.

Ehrke MJ, Cohen SA, Mihich E
Dept. Experimental Therapeutics and Grace Cancer Drug Center, Roswell Park Memorial Inst., Buffalo, NY, 14263
Immunol Rev; 65:55-76 1982

Effects of adriamycin (ADM) on allogeneic cell mediated cytotoxic (CMC) and phagocytic response, modification of responses to syngeneic tumor, modulation of the humoral responses, and effects of ADM on natural killer (NK) activity are discussed. Effect of ADM on the response of C57B1/6 spleen cells against P815 mastocytoma was evaluated using a 4-hr 51Cr release assay at the end of the 'effector development' stage. Effector cells involved in the ADM-augmented cytotoxic activity after culture were shown to be associated with cells both adherent and non adherent to plastic, insensitive to addition of silica 24 hr prior to assay, and eliminated following addition of anti-Thy 1.2 plus complement. No difference in crystallizable fragment (Fc) dependent phagocytic activity was observed with uncultured spleen cells from untreated mice or mice treated with ADM 1 or 5 days prior to sacrifice. Results were consistent with the suggestion that the necrosis observed 1 day after treatment with ADM involved an immature monocyte population in the spleen. According to results ADM does not affect CMC responses by selectively interacting with T-helper or T-suppressor cells. Administration of ADM (5 mg/kg, iv) to mice 5 days prior to inoculation with P815 cells resulted in either no effect or augmentation of the CMC response depending upon dose of antigen or day of assay. ADM, in general, inhibited humoral responses and NK activity when tested under conditions which led to an augmented CMC. (68 Refs)

## 41. IMPAIRED PWM-INDUCED POLYCLONAL B-CELL ACTIVATION IN PATIENTS WITH MALIGNANCIES TREATED WITH VARIOUS INTERMITTENT COMBINATION CHEMOTHERAPIES INCLUDING DOXORUBICIN.

Horino N
Dept. Pediatrics, Natl. Center Cardiovascular Disease, Fujishiro-dai, Suita, Osaka Prefecture, Japan
Cancer; 50(4):659-667 1982

The effect of various intermittent combination chemotherapies on the immune status of 30 patients with malignancies was examined 1-3 wk after they received their last injection. PWM-induced polyclonal B-cell activation of lymphocytes from patients treated with combination chemotherapies that included doxorubicin was impaired despite a normal 3H-thymidine uptake by lymphocytes stimulated with PHA, PWM, and insoluble SPA. This suppressive effect was always found in patients with ALL. However, in patients with solid tumors, PWM-induced immunoglobulin production returned to normal 7-8 wk after the last doxorubicin injection. Serum immunoglobulin levels in patients treated with doxorubicin were slightly lower than in those treated without doxorubicin. It is hypothesized that doxorubicin may change the lymphocyte surface membrane and interrupt the T- and B-cell interaction that is needed for immunoglobulin production. (Author abstract) (21 Refs)

## 42. EFFECTS OF DIPHENYLHYDANTOIN ON KILLER CELL ACTIVITY AND OTHER IMMUNOLOGICAL FUNCTIONS. A SEQUENTIAL STUDY INCLUDING THE INTERACTION OF CORYNEBACTERIUM PARVUM IN MELANOMA PATIENTS.

Thatcher N, Wan HH, Swindell R, Wilkinson PM, Crowther D
Dept. Medical Oncology, Christie Hosp. and Holt Radium Inst., Wilmslow Road, Manchester M20 9BX, England
Int J Immunopharmacol; 4(3):167-174 1982

The effects of a single dose of phenytoin (PHEN; 300 mg/square meter) upon killer cell (NK) cytotoxicity, serum immunoglobulins, and T and B cell proportions was investigated prospectively in 11 patients (6 males, 5 females) with metastatic malignant melanoma. No acute change in T lymphocyte rosettes, serum immunoglobulins, and DNA synthesis of lymphocyte cultures were observed after PHEN treatment. An early immunosuppression occurred within 10 hr after PHEN with reductions in lymphocyte count and NK activity. This suppression was reversible, with apparent recovery by 58 hr. Such a feature could explain the transient lymphadenopathy observed before cessation of PHEN medication. The profound and early immunosuppression associated with the first PHEN dose was abrogated by Corynebacterium parvum immunization (iv infusion 2 mg/square meter in 300 ml physiological saline over 3 hr) preceding a second dose of PHEN. While the second dose of PHEN caused some immunosuppression, no increase in T cells, NK, and phytohemagglutinin induced cytotoxicity above initial values was observed. (23 Refs)

## 43. EFFECT OF THERAPY ON T CELL SUBPOPULATIONS IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA.

Kay NE, Howe RB, Douglas SD
(c/o Douglas) Div. Allergy-Immunology, Children's Hosp. Philadelphia, 34th and Civic Center Blvd., Philadelphia, PA, 19104
Leuk Res; 6(3):345-348 1982

Fifteen chronic lymphocytic leukemia (CLL) patients were studied at various stages of the disease in order to delineate more closely the significance of imbalance in the T cell subsets in CLL. All patients studied were diagnosed as B cell type of CLL by clinical presentation and use of surface immunofluorescence staining procedures. The stage of each patient was determined by the Rai classification system. T cell studies were performed prior to chemotherapy or 3-4 wk post-therapy. An increase above control in the mean value of total T cells, a significant increase in Tgamma cells, and a pronounced decrease in CLL Tmu cells over control were observed. The early stage patients had lower numbers of Tgamma cells than advanced patients but were still significantly above the level in controls although one patient was in the control range. The in vitro appearance of Tmu cells for early patients was greater than that of advanced group, but only one patient was in the control range (control mean Tmu 2,010 +-195). Three advanced patients were studied immediately prior to and 7-10 days after splenectomy. All three patients demonstrated significant reductions from the pre-operative absolute Tgamma cell concentration. No change was noted in the ability to develop Tmu cells in vitro. In all three patients the removed spleens were diffusely involved with malignant lymphocytes. The decrease in the proportion of Tgamma cells after splenectomy and the increase in Tgamma cells in progressive disease post-splenectomy suggested that Tgamma cells may be an important determinant of the course of CLL. (16 Refs)

## 44. COOPERATIVE ROLE OF T LYMPHOCYTES AND MACROPHAGES IN ANTI-TUMOR ACTIVITY OF MICE PRETREATED WITH SCHIZOPHYLLAN (SPG).

Suzuki M, Arika T, Amemiya K, Fujiwara M
Central Res. Lab., Kaken Chemical Co., Ltd., Honkomagome, Bunkyo-ku, Tokyo 113, Japan
Jpn J Exp Med; 52(2):59-65 1982

Anti-tumor activity against Sarcoma-180 was studied in female jcl:ICR mice injected ip with schizophyllan (SPG), a glucan produced by Schizophyllum commune. Anti-tumor activity was transferrable into normal mice by lymph node cells of animals pretreated with SPG and lasted up to 60 days after SPG administration to donor mice. In vitro treatment of SPG-treated lymph node cells with anti-Thy-1.2 sera and complement abolished the anti-tumor activity. Spleen cells from SPG-treated mice induced anti-tumor activity up to 10 days, but lost effectiveness by 60 days. Delayed cutaneous hypersensitivity reaction with picryl chloride was enhanced in mice receiving lymph node cells form SPG-treated donor mice; such enhancement was not observed when spleen cells were used. In vivo treatment with inhibitors of macrophage function (trypan blue and carageenan) reduced the anti-tumor activity of SPG in injected mice and decreased the effectiveness of transferred spleen or lymph node cells. The anti-tumor activity in SPG-treated mice apparently derived both from activated macrophages and T-cells in the lymph node or spleen. The T-cells and macrophages may cooperate in each other's activation. (11 Refs)

## 45. KINETICS OF ACTIVATION OF MACROPHAGES INDUCED BY DIMETHYLDIOCTADECYLAMMONIUM BROMIDE (DDA) (MEETING ABSTRACT).

Prager MD, Baechtel FS, Farmer JL, Gordon WC, Mauldin S, Steinberg J, Vanderzee J
University of Texas Health Science Center, Dallas, TX, 75235
Proc Am Assoc Cancer Res; 23:1033 1982

With tumor associated antigen (Ag), DDA stimulates murine anti-tumor responses in immunoprophylaxis and chemoimmunotherapy protocols. DDA effects are mediated by at least two processes: 1) complexing with Ag so as to present modified Ag to the immune system, and 2) macrophage activation as judged by a variety of parameters. The kinetics of parameter alteration for murine peritoneal macrophages following ip DDA injection has been investigated. Enhanced Fc receptor activity was observed day 1 after DDA and remained elevated through day 4. Peroxidase (cytochemical) was barely detectable on day 0, became strong on day 2, and dropped to pre-injection levels on day 4. The lysosomal enzymes beta-glucuronidase (betaG) and acid phosphatase (AP) were increased on day 2, peaked on day 3, and gradually declined over the next week. The maximum increase for betaG and AP was 3 and 12-fold/cell, respectively. Although betaG exhibited no increase in specific activity, that for AP increased 5-fold, indicating specific induction. The cytosolic enzyme lactic dehydrogenase presented a pattern like that of betaG. The effect of DDA induced macrophages on growth of one mouse and 2 human leukemic cell lines has been evaluated by cell enumeration. Relative to resident macrophages, day 4 DDA induced cells inhibited growth, but the leukemic cells exhibited variable sensitivity to macrophage attack. It is clear that these parameters by which macrophage activation is judged follow quite different kinetics. (no Refs)

## OTHER RELATED STUDIES

### 46. CIRCULATING SUPPRESSOR MONOCYTES IN MALIGNANT DISEASE.

**Berlinger NT**
**University of Minnesota, Minneapolis, MN**
**Diss Abstr Int [B]; 42(10):4008-B 1982**

T-lymphocyte proliferation in mixed leukocyte culture was measured for normal individuals and for patients with squamous cell carcinoma of the head and neck. Normal responsiveness calculated by the relative response method was established to be 68% or greater. Cancer patients frequently showed abnormally low levels of T-cell proliferation. When patient macrophages were removed from the mixed cell cultures, significantly increased levels of T-cell proliferation often occurred in previously poorly reactive cultures. Macrophages were removed by filtering patient peripheral blood leukocytes through columns of Sephadex G-10 beads. Fractions of irradiated immune cells were added back to mixed cell cultures of patient macrophage-depleted lymphocytes which showed significantly increased T-lymphocyte proliferation after macrophage removal. The fractions which were depleted of macrophages by G-10 column filtration or which were enriched to T-cells by rosetting with sheep erythrocytes showed no significant suppression of T-lymphocyte proliferation. The fraction which did not rosette with sheep erythrocytes showed significant suppression of T-lymphocyte proliferation as did unseparated peripheral blood leukocytes. In short only those fractions which contained macrophages or were enriched for macrophages showed any evidence of suppression of autologous patient T-cells. Cancer-free individuals from family aggregates of seemingly hereditary colon cancer were similary studied and some also showed evidence of suppressor macrophages. This indicated that the appearance of the suppressive cell in some instances could perhaps antedate the appearance of a tumor. Macrophages of normal individuals also was able to suppress autologous T-lymphocyte proliferation in mixed leukocyte culture. However, macrophages from cancer patients were significantly more efficient suppressor cells, indicating that excessive macrophage suppression with cancer may be a perturbation of a normal homeostatic mechanism. (no Refs)

### 47. NEW CYTOGENETICS FINDINGS IN A PATIENT WITH ACUTE PROMYELOCYTIC LEUKEMIA (APL) (MEETING ABSTRACT).

**Rodriguez S, Verma RS, Dosik H**
**Department of Medicine, The Jewish Hospital and Medical Center of Brooklyn, Brooklyn, NY**
**Am J Hum Gen; 33(6):67A 1982**

Besides the clinical and morphological features, a specific association with a unique chromosome translocation t(15q+;17q-) is recognized in patients with acute promyelocytic leukemia (APL). We present a case where chromosomal abnormalities are not distinctive for APL. A 19 year old male was diagnosed as having APL. Complete blood count on admission showed hemoglobin 16.6 gm/dl; hematocrit 48%, platelets 133 x 10(9)/liter; and white cells, 4100/mm3, with a differential of 7% blasts, 32 promyelocytes, 4% myelocytes, 13% granulocytes, 8% monocytes, 36% lymphocytes. A bone marrow aspiration was done which showed blasts 10% promyelocytes 72%, granulocytes 12%, lymphocytes 2%, erythroid precursors 2% and plasma cells 2%. It is necessary to review the morphological features of all cases of APL and compare them with chromosomal changes. Cytogenetic analysis was performed on 12/11/80 and three consistent markers were found: M1(t(11q;1q)), M2(t(6p;13q)), M3(i(17q)) with the loss of Y chromosome from his bone marrow aspirate. Ninety percent cells were abnormal while 10% of the cells were cytogenetically normal. A second aspirate was done on 3/2/81 and the same three markers were noted. However, both chromosome number Is were normal, suggesting a secondary cytogenetic change in the patient. (no Refs)

### 48. IMMUNOTHERAPY OF TRANSPLANTED MURINE LEUKEMIAS BY MONOCLONAL ANTIBODY (MCAB) (MEETING ABSTRACT).

**Kirch ME, Abbott J, Lee T, Hammerling U**
**Sloan-Kettering Institute, New York, NY, 10021**
**Fed Proc; 41(3):367 1982**

Murine T cell-derived leukemias have been transplanted into hosts congenic for T lymphocyte differentiation antigens (LDA). McAb directed at the LDA (Thy 1 or Lyt 2) were evaluated for their ability to abrogate tumor growth in vivo. Intraperitoneally injected IgG3 anti-Thy 1.2 McAb was extremely effective in curtailing the growth of subcutaneously inoculated ASL.1 cells (growing in A/Thy 1.1 hosts) if the antibody was administered within 24 hours of the tumor. Between 24 and 48 hours, the tumor becomes refractory to therapy, a fact that is not attributable to differences in the number of tumor cells present. IgM antibody extended survival time, but did not cure regardless of the status of the host with respect to hemolytic complement levels. In other studies, anti-Lyt 2 was effective in therapy of ERLD, but not EL4 when these B6-derived tumors were transplanted into B6/Lyt 2.1 hosts. The results with ASL.1 indicate that C-mediated cytolysis is not required for therapy, and in no case does an endogenous immune response appear to contribute to abrogation of tumor growth by McAb. Anti-Thy 1.2 McAb inhibits proliferation of ASL.1 in culture, and it is possible that antibody exerts its effects in vivo without recourse to host effector functions. Antibody-dependent cellular cytotoxicity may also contribute to therapy. (no Refs)

### 49. ON CERTAIN IMMUNOLOGICAL INDICES IN PATIENTS WITH LOCAL NEOPLASMS OF HEAD AND NECK.

**Bulbuk GA**
**Res. Inst. Oncology Moldavian SSR, Kishinev, USSR**
**Vopr Onkol; 28(4):57-59 1982**

The study is concerned with the functional state of lymphocytes, granulocytes and levels of immunoglobulins IgG, IgA and IgM in blood serum of patients with local neoplasms of the pharynx, thyroid, oral cavity and tongue. Cancer patients revealed a considerable decrease in the levels of rosette-forming T-lymphocytes, plaque-forming cells and granulocytes, capable of reducing nitroblue tetrazolium, blood serum levels of IgG, IgA and IgM being practically unchanged. There is a relationship between the type of clinical course of disease and severity of immunological disorders in advanced cancer of the pharynx. Immunologic response disturbances are most manifest, when immune surveillance is undermined by tumor process and metastasis development. (Author abstract) (6 Refs) (In RUS)

## 50. INHIBITION OF CYTOKINE PRODUCTION BY A TUMOUR CELL PRODUCT.

**Farram E, Nelson M, Nelson DS, Moon DK**
**(c/o Nelson, D. S.) Kolling Inst. Medical Res., Royal North Shore Hosp., St. Leonards, NSW 2065, Australia**
**Immunology; 46(3):603-612 1982**

Supernatants from cultured mouse and human tumor cells, but not mouse or guinea-pig fibroblasts, inhibited the production of a lymphokine, macrophage chemotactic factor, by PHA-stimulated mouse spleen cells. The supernatants affected spleen cells from old, but not young, mice. They were most active if added at the start of the spleen cell culture and did not act by binding phytohemagglutinin (PHA). The active material had an approx mol wt, on membrane filtration, of 1,000-10,000 and could be bound to and eluted from Con A-Sepharose. Tumor supernatant factor(s) of similar mol wt inhibited the production of interleukin 1 (lymphocyte activating factor) in response to lipopolysaccharide by stimulated thioglycollate-induced peritoneal exudate macrophages, but not by Corynebacterium parvum-activated macrophages. Similar tumor-produced material has been found to inhibit the early phase of delayed-type hypersensitivity reactions in older mice. It is suggested that this effect is due, at least in part, to inhibition of interleukin 1 production leading to inhibition of lymphokine production. (Author abstract) (26 Refs)

## 51. IMMUNOSUPPRESSION RELATED TO ASCITIC FLUID IN PATIENTS WITH OVARIAN CARCINOMA.

**Marotti T, Hrsak I, Krusic G, Deveric G**
**Dept. Experimental Biology and Medicine, Ruder Boskovic Inst., P.O. Box 1016, Bijenicka 54, 41001 Zagreb, Yugoslavia**
**Oncology; 39(5):298-303 1982**

The immune response to SRBC (PFC assay) was suppressed in mice injected with cell-free ascitic fluid from patients with ovarian carcinoma. The immunosuppressive effect of ascitic fluid obtained from Stage IV patients was stronger than that of Stage III patients. These data were correlated with the patient's immune status (number of E and EAC rosettes, PHA reactivity of lymphocytes, skin reactivity to recall antigens) and with changes in protein fractions in the serum and ascitic fluid. A good correlation was found between the immunosuppressive effect in the mouse PFC assay and the increased quantity of alpha-1-globulins in ascites. Skin nonreactivity to PPD also correlated with the immunosuppressive effect of ascitic fluid. However, the lymphocyte response to PHA and the numbers of E and EAC rosettes did not correlate either with skin reactivity to recall antigens or with the suppression of PFC response in mice. (Author abstract) (20 Refs)

## 52. LACK OF SPECIFICITY FOR VIRAL AND H-2 ANTIGENS BY ANOMALOUS T KILLER CELLS GENERATED IN MURINE LEUKOCYTE CULTURES.

**Shain B, Holt CA, Lilly F**
**Dept. Genetics, Albert Einstein Coll. Medicine, Bronx, NY, 10461**
**J Immunol; 129(2):722-729 1982**

Mouse spleen cells, cultivated in vitro for 6 days in the presence or absence of syngeneic irradiated virus-induced tumor cells, lysed a variety of virus-induced tumor cells and normal cells in a long (19-hr) 51Cr-release cytotoxicity assay. Little or no specificity for viral or H-2 antigens was detected. This anomalous killing (AK) activity contrasted with H-2-restricted cytotoxic T lymphocyte (CTL) activity generated in secondary mixed leukocyte-tumor cell cultures and detected in a short (4- to 6-hr) 51Cr-release assay. Studies of competitive inhibition by unlabeled target cells in the long assay suggested that AK effectors were a broadly heterogeneous mixture of cells representing many clones, each recognizing a different antigenic determinant. AK effector cells shared properties with CTL: they could be generated from spleen cells of natural killer cell-deficient mice bearing the beige mutation but not from those of T cell-deficient nude mice; they expressed Thy-1 and Lyt-2 antigens; and they were nonphagocytic. AK activity could be generated from normal spleen cells of mice of all inbred strains examined, but the levels of activity generated varied in a strain-specific manner and were not significantly influenced by H-2 genotype. (Author abstract) (50 Refs)

## 53. IN VIVO INHIBITON OF MOUSE LEUKEMIA BY CYTOTOXIC T-CELL CLONES AND EXOGENOUS IL-2 (MEETING ABSTRACT).

**Palladino MA, Old LJ, Oettgen HF**
**Memorial Sloan-Kettering Cancer Center, New York, NY, 10021**
**Fed Proc; 41(3):406 1982**

T-cell clones specific for a unique surface determinant on BALB/c RL male1 were derived from spleens of CB6F1 mice immunized in vivo and in vitro with RL male1. The reactive cells were expanded in IL-2 containing media and cloned by limiting dilution at less than .5 cells/well. Specificity was determined by direct and competitive inhibition assays. Cytotoxicity at the effector level was blocked by Lyt-2.2 and 3.2 but not by Lyt-1.2, Ly-5.1 or Thy-1.2 antisera and at the target level with H-2Dd but not H-2b antisera. CB6F1 mice inoculated intradermally with 10(6) RL male1 were injected intraperitoneally with 10(7) cytotoxic T-cells every other day for a total of 3 injections with 100-200 units of IL-2. Subcutaneous growth of RL male1 in mice receiving T-cells and IL-2 was delayed compared to mice receiving IL-2 alone (.23 cm vs .53 cm on day 9), and survival was prolonged (69% vs 45% on day 28). Winn tests showed that the transferred T-cell clones maintained their specificity for the unique antigen of RL male1. We conclude that cytotoxic T-cell clones may be effective agents of adoptive immunity. (no Refs)

## 54. NATURAL CELL-MEDIATED CYTOTOXICITY IN VITRO AND INHIBITION OF TUMOR GROWTH IN VIVO BY MURINE LYMPHOID CELLS CULTURED WITH T CELL GROWTH FACTOR (TCGF).

**Kedar E, Ikejiri BL, Gorelik E, Herbermann RB**
**(c/o Herbermann) Lab. Immunodiagnosis, NCI, NIH, Bethesda, MD, 20205**
**Cancer Immunol Immunother; 13(1):14-23 1982**

Characteristics of mouse cultured lymphoid cells (CLC) derived from lymphoid cells of normal and tumor-bearing mice were examined, and their cytotoxic reactivity against a variety of lymphoid and solid tumors was assessed. Lymphoid cells obtained from the spleen of normal and tumor-bearing mice were cultured for various periods of time, in different culture vessels, in the presence of crude or mitogen-depleted T cell growth factor (TCGF) of mouse and rat origin. The growth pattern of various cultures was monitored 3x/wk by viable cell counting, and the results obtained with some of the splenocyte cultures are shown. All CLC cultures maintained by the periodic addition of TCFG showed a strong cytotoxic activity against most of the tumor target cells tested: fresh and cultured, syngeneic and allogeneic, lymphoid and solid, natural killer (NK)-sensitive and NK-resistant. Cultured M109 and MT were slightly more sensitive to killing, in general, than freshly harvested transplanted M109 or primary spontaneous MT.

With most of the CLC, max cytotoxic activity was observed after 2-3 wk in culture. Several surface markers that have been associated with either cytotoxic T lymphocytes or NK cells were assessed. Results suggested that Thy 1.2 is present on the CLC at a lower density or is less accessible to antibody plus complement attack than on fresh T cells. In local Winn neutralization assays, BALB/c CLC afforded partial protection against a syngeneic lymphoma and carcinoma (M109) in BALB/c mice and against an allogeneic lymphoma (MBL-2) in C57BL/6 mice. Systemic administration of CLC to mice with established disseminated tumors showed a limited therapeutic effect in two experiments. (39 Refs)

## 55. INTERLEUKIN STIMULATION OF PROLIFERATION AND DIFFERENTIATION IN NEOPLASTIC HUMAN B CELLS (MEETING ABSTRACT).

**Ford RJ, Morgan J, Scouros M, Mehta S, Lachman L, Maizel AL**
**Department of Pathology, University of Texas, M. D. Anderson Hospital, Houston, TX, 77030**
**Fed Proc; 41(3):419 1982**

Neoplastic human B cell were obtained from either lymph nodes or spleens from patients with non-Hodgkin's lymphomas (NHL) or from the peripheral blood of patients with chronic lymphocytic leukemia (CLL). The neoplastic cells were enriched by T cell and adherent cell depletion, and characterized as B cell type by the presence of surface Ig and as monoclonal by light chain typing. Non-neoplastic cells were less than 5% by comprehensive marker analysis. These tumor cell populations were assayed for proliferation after stimulation with lectin-free DEAE (diethylaminoethyl)-purified IL-2 preparations containing normal T cell and B cell growth factors. IL-2 preparations stimulated both 3H-Tdr (thymidine) incorporation and cell growth but not Ig secretion in both NHL and CLL cells. Purified Interleukin-I did not stimulate either proliferation or differentiation alone, but in some cases stimulated Ig synthesis in the presence of autologous or allogeneic purified T cells. In addition, both NHL and CLL cells could be grown in vitro for extended periods in IL-2 preparations, while control cultures without IL-2 died out within 7 days. These studies imply that at least some neoplastic B cells retain sensitivity to accessory cell helper factors, which may regulate the growth of some neoplastic cells. (no Refs)

## 56. FUNCTIONAL PROPERTIES OF UV1: A CONTINUOUS T-SUPPRESSOR CELL LINE WITH TUMOR SPECIFICITY (MEETING ABSTRACT).

**Roberts LK, Spellman CW, Warner NL**
**Department of Pathology, University New Mexico School of Medicine, Albuquerque, NM, 87131**
**Fed Proc; 41(3):478 1982**

A continuous T-suppressor cell line (UV1) has been derived from a Balb/c mouse irradiated with a subcarcinogenic dose of ultraviolet light (UV). UV1 was established by placing nylon wool non-adherent splenocytes directly into tissue culture, supplemented with interleukin 2, without exogenous antigenic stimulation. This cell line has been cloned and maintained in exponential growth culture for approximately 10 months. UV1 expresses a number of T-cell antigens, including Thy 1.2, and is negative for various B-cell and macrophage markers, as well as Lyt, 1, 2 and 3, by FACS analysis. Functionally, UV1 injected either intravenously or intraperitoneally renders mice susceptible to the growth of UV-regressor tumors. These tumors are rejected when implanted into normal syngeneic hosts that lack a state of UV-induced tumor-specific suppression. UV1 also enhances the growth rate of UV-progressor tumors. In addition to its in vivo activity, UV1 is also capable of in vitro function. Cytotoxic T-lymphocytes (CTL) differentiate after 4 days in tissue culture from the draining lymph nodes (DLN) of UV-tumor immune mice. This CTL conversion can be effectively blocked by co-incubating DLN cells with UV1. It appears that UV1 has functional specificity for common tumor associated antigens. This continuous cell line will now allow us to study various host-tumor interactions that result in either tumor growth or rejection. (no Refs)

## 57. INTERLEUKIN 1 ENHANCES PHORBOL ESTER STIMULATED PRODUCTION OF INTERLEUKIN 2 AND COLONY STIMULATING FACTOR BY A MOUSE THYMOMA CELL LINE (MEETING ABSTRACT).

**Hilfiker ML, Moore RN, Sando JJ**
**Cleveland Clinic Foundation, Cleveland, OH, 44106**
**Fed Proc; 41(3):563 1982**

Interleukin I (IL 1) has been reported to enhance mitogen-induced production of T cell growth factor (Interleukin 2: IL 2) by mouse spleen cells. We have investigated this relationship between IL 1 exposure and production of factors by stimulated T cells using, as a model system, a mouse thymoma cell line, EL 4. Phorbol 12-myristate, 13-acetate (PMA) alone promotes IL 2 and colony stimulating factor (CSF) production by EL 4 cells and concomitantly inhibits proliferation of these cells. We have now demonstrated that partially purified IL 1 alone does not affect EL 4 proliferation or production of IL 2 and CSF; however, in the presence of PMA, IL 1 enhances, in a dose-dependent manner, both IL 2 and CSF production 2-3 fold and lowers the threshold dose of PMA needed to stimulate factor production. Similarily, IL 1 enhances Con A (concanavalin A) stimulated production of IL 2 and CSF by EL 4 cells. IL 1 may act during the initial phases of stimulation of production since incubation of EL 4 cells with IL 1 for 2 or 6 hr, followed by washing, and then stimulation with PMA leads to a 2 fold enhancement of IL 2 and CSF production. The possibility that incubation of EL 4 cells with IL 1 may affect the number of affinity of PMA receptors and thus account for the synergistic action of these agents is being investigated. (no Refs)

## 58. PHASE I TRIALS OF THYMOSIN FRACTION 5 (TF5) AND THYMOSIN ALPHA (TA1) AND ASSESSMENT OF IMMUNOLOGIC RESPONSE (MEETING ABSTRACT).

**Dillman RO, Beauregard JC, Zavanelli MI, Halliburton BL, Royston I**
**University of California, San Diego Cancer Center, School of Medicine, San Diego, CA, 92161**
**Proc Am Soc Clin Oncol; 1:C-166 1982**

TF5 and TA1 were tested as part of the Biological Response Modifiers Program. Seventy-two patients with advanced cancer were screened for immunosuppresion using a battery of cell surface markers and lymphocyte function assays. Marker studies included proportion and number of lymphocytes, T cells by E-rosettes and monoclonal antibodies, helper and suppressor cells and Ia+ cells by monoclonal antibodies, B cells by surface immunoglobulin. Functional assays included phytohemagglutinin, concanavalin-A, pokeweed mitogen, one-way mixed lymphocyte reactions to human lymphocytes and cell lines, and response to viral antigen (varicella-zoster). As a group, cancer patients had statistically lower means for 16/21 in vitro tests of immunosuppression as compared to healthy controls. Over 2/3 of cancer patients were determined to be immunosuppressed. The ratio of helper/suppressor cells was less than 1:1 in half of the cancer patients, but in less than 10%

of controls. Twenty-two patients received 30 courses of single intramuscular injections of TF5 or TA1 according to a doubling dose escalation schedule. Such patients were tested on 3 occasions before receiving thymosin, then daily X 3 and weekly X 3 after the injection. Results can be summarized as follows: (1) TF5 and TA1 were well tolerated over the dose range of 60-480 mg/m2 and 600 ng to 9.6 mg/m2 respectively; (2) any effects of TF5 or TA1 on various assays were seen within 24-48 hours and did not persist beyond 72 hours; (3) there was marked variation in terms of immune response; and (4) no dose-response correlation was apparent. (no Refs)

## 59. AUGMENTATION OF HUMAN NATURAL KILLER CELLS BY ALPHA-INTERFERON, AND GAMMA-INTERFERON INDUCERS. ANALYSIS BY MONOCLONAL ANTIBODIES (MEETING ABSTRACT).

**Platsoucas CD**
**Memorial Sloan-Kettering Cancer Center, New York, NY, 10021**
**Fed Proc; 41(3):957 1982**

Natural killer (NK) cells in humans are phenotypically heterogeneous. They express the following antigens: T11a (the receptor for sheep erythrocytes), T10 (present on early T cells, prothymocytes and plasma cells) and M1 (present on monocytoid cells). Using a panel of monoclonal antibodies, we investigated the population of human peripheral blood NK cells than can be augmented by in vitro treatment with human leukocyte interferon (IFN-alpha) or staphylococcal enterotoxin A (SEA; a gamma-interferon inducer). In vitro treatment with IFN-alpha resulted in significant augmentation of NK mediated by purified (by fluoresence activated cell sorting) OKT11a-positive. 9.6-positive or OKM1-positive cells. Depletion experiments using the OKM1 antibody and complement (C) suggested that IFN-alpha augments both M1-positive or M1-negative cells. Treatment of monocyte-depleted lymphocytes with OKT11a and C resulted in substantial reduction (by 40 to 70%) of the augmentation of NK by IFN-alpha. Depletion of T11a-positive or M1-positive cells did not prevent highly significant augmentation of NK by SEA treatment. In other experiments we investigated the cell surface phenotypes of human NK cells after in vitro treatment with IFN-alpha or SEA. NK augmented by IFN-alpha was significantly reduced after removal of T10-positive (by 80 to 90%) or T11a-positive cells (by 60 to 80%) and partially after removal of M1-positive cells (40 to 60%). NK augmented by SEA was only partially reduced by depletion of T10-positive (by 50%) or T11a-positive cells (by 50%) and was not affected by depletion of M1-positive cells. These results suggest that human NK cells are a heterogenous and complex system and their different populations may be augmented to different extent by various biological response modifiers. (no Refs)

## 60. PURIFICATION OF HUMAN BONE MARROW (BM) CELLS PRIOR TO TRANSPLANTATION (MEETING ABSTRACT).

**Vriesendorp H, Gordon LI, Kies MS, Kucuk O, Prachand S, Visser T**
**Northwestern University, Chicago, IL, 60611**
**Proc Am Soc Clin Oncol; 1:C-734 1982**

Human BM cells were separated into four fractions using a discontinous bovine albumin gradient in an effort to concentrate hemopoietic stem cells and remove T lymphocytes or tumor cells. BM was obtained from 35 normal human volunteers, 3 patients (pts) with multiple myeloma (MM), 2 pts with small cell carcinoma of the lung (SCCL) and 3 pts with metastatic breast carcinoma (BC). BM fractions were analyzed for granulocyte-macrophage colony forming units (CFUc), tumor colony forming units (TFUc), phytohemagglutinin (PHA) response and rosette formation with sheep erythrocytes (SRBC). A 9 fold increase in CFU concentration and over 75% of total CFUc were found in low density fraction 3, which also was PHA negative and contained 20% of the total number of SRBC rosette forming cells. After conditioning with radiation and cyclophosphamide, engraftment was obtained in two patients with chemotherapy resistant acute leukemia with 3 x 10(7) cells/kg body weight from fraction 3. No prophylactic methotrexate was given. Histological signs of moderate graft-vs-host disease were observed within a month after BMT. In further experiments with normal human BM additional T lymphocyte removal was obtained by rosetting fraction 3 cells with SRBC. The non-rosetting fraction contained 80-100% of the total CFUc and less than 1% of the total rosette forming cells. In cancer pts BM TCFUc were isolated primarily in heavier fraction 4 in MM or lighter fraction 1 + 2 in SCCL and BC while CFUc remained in fraction 3. (no Refs)

# AUTHOR INDEX WITH CITATION NUMBERS


Abbott J. 48
Altman A. 13
Altman LC. 33
Amemiya K. 44
Arika T. 44
Baechtel FS. 45
Baum LL. 14
Beauregard JC. 58
Bennett P. 10
Berlinger NT. 46
Beveridge RP. 7
Billing RJ. 1
Blackledge G. 25
Brochier J. 9
Bulbuk GA. 49
Burns ER. 16
Cadoni A. 29
Cantor H. 26
Carson DA. 13
Cauchy L. 24
Clynes M. 31
Coffey T. 4
Cohen SA. 40
Comis R. 28
Corrigan A. 31
Coudert F. 24
Crowther D. 25
Crowther D. 42
Czernielewski J. 9
Dambrine G. 24
Davey F. 28
Davis F. 12
De Heer E. 22
De Weger RA. 22
Den Otter W. 22
Deveric G. 51
Dillman RO. 58
Dosik H. 47
Douglas SD. 43
Dullens HF. 22
Dvorak AM. 26
Dvorak HF. 26
Ehrke MJ. 40
Elion GB. 37
Farmer JL. 45
Farram E. 50
Ferrarini M. 29
Fjelde A. 10
Foon KA. 1
Foon KA. 2
Ford RJ. 12
Ford RJ. 55
Fujiwara M. 44
Gale RP. 2
Gallaher J. 25
Galli SJ. 26
Ganul VL. 38
Gewurz H. 14
Ginsberg S. 28
Glukhen'kaia GT. 38
Gordon LI. 60
Gordon WC. 45
Gorelik E. 54
Griffin JD. 7
Grinevich IuA. 38
Grogan TM. 11
Grossi CE. 29
Grossmayer B. 20
Halliburton BL. 58
Halper JP. 39
Hammerling U. 48
Hartley JW. 36
Heinrichs H. 18
Herbermann RB. 54
Herrlich P. 30
Hicks MJ. 11
Hilfiker ML. 57
Hilgers J. 22
Holt CA. 52
Horino N. 41
Howe RB. 43
Hrsak I. 51
Hurtubise PE. 8
Ikejiri BL. 54
Ishizaka T. 26
James K. 14
Jolley CS. 11
Jones S. 11
Kamenets LIa. 38
Kay NE. 43
Kedar E. 54
Kellam J. 10
Kies MS. 60
Kirch ME. 48
Klimpel GR. 33
Kogut GI. 38
Krusic G. 51
Kucuk O. 60
Kusyk C. 12
Lachman L. 55
Lachman LB. 12
Lakow E. 13
Layton JM. 11
Lee T. 48
Lemaire G. 27
Lepoivre M. 27
Leprini A. 29
Lilly F. 52
Linker-Israeli. 1
Liu JS. 15
Maizel AL. 12
Maizel AL. 55
Mallick U. 30
Marcus JN. 8
Marotti T. 51
Mauldin S. 45
Medzihradsky J. 37
Mehta S. 55
Mendelsohn J. 6
Meyers PA. 5
Mier J. 28
Mihich E. 40
Miller DR. 5
Mohanakumar T. 4
Moon DK. 50
Moore RN. 57
Morgan J. 12
Morgan J. 55
Morse HC. 36
Muller C. 18
Nabel G. 26
Namikawa R. 3
Narula N. 5
Negoro T. 19
Nelson DS. 50
Nelson M. 50
Nishida K. 3
Nishizuka Y. 3
Nussbaum-Blumen. 20
O'Kennedy R. 31
O'Malley J. 20
Oettgen HF. 53
Ogata SI. 3
Okulov LV. 38
Old LJ. 53
Ota K. 3
Ozer H. 20
Pahwa R. 5
Palladino MA. 53
Pernis B. 39
Peterman GM. 33
Petit JF. 27
Pistoia V. 29
Platsoucas CD. 59
Poiesz B. 28
Ponta H. 30
Prachand S. 60
Prager MD. 45
Pretlow TG. 17
Pretlow TP. 17
Price JA. 35
Quinn RP. 37
Quiroga LE. 8
Rahmsdorf HJ. 30
Raphael L. 15
Richardson D. 6
Roberts LK. 56
Rodriguez S. 47
Roholt O. 10
Roth P. 39
Royston I. 58
Royston I. 6
Rudolph A. 28
Ruscetti F. 28
Russell EC. 4
Saji F. 19
Sando JJ. 57
Schlossman SF. 7
Schmitt D. 9
Schroff RW. 2
Scouros M. 55
Shain B. 52
Sheedy D. 20
Shenouda G. 34
Simonian HD. 26
Smith RE. 35
Smyth H. 31
Soufleris AJ. 17

Souteyrand P. 9
Spellman CW. 56
Stanton GJ. 33
Steinberg J. 45
Steinke B. 18
Suzuki M. 44
Swindell R. 42
Taetle R. 6
Takahashi T. 3
Tanigaki N. 19
Tanimoto M. 3
Tenu JP. 27
Teplow DB. 21
Thatcher N. 42
Thivolet J. 9
Thomson DM. 34
To D. 6
Tom BH. 15
Ueda R. 3
Valentine F. 16
Van Basten CD. 22
Vanderzee J. 45
Verma RS. 47
Vetter ML. 14
Visser T. 60
Vose BM. 25
Vriesendorp H. 60
Waller HD. 18
Wan HH. 42
Warner NL. 56
Weinhold KJ. 23
Weinstein IB. 39
Wernet P. 18
Wheelock EF. 23
Wilkinson PM. 42
Wolberg G. 37
Word CJ. 32
Zamkoff K. 28
Zavanelli MI. 58
Zicca A. 29
Ziegler A. 18
Zucker-Franklin. 16



☆ U.S. GOVERNMENT PRINTING OFFICE: 1982-381-847:205

# NEW ONCOLOGY OVERVIEWS ON CARCINOGENESIS

The following are titles of retrospective bibliographies that contain 100-500 selected abstracts of recent cancer research publications on carcinogenesis topics. Additional Oncology Overview titles are also available for the Cancer Diagnosis and Therapy Series and the Cancer Virology/Immunology/Biology Series; these titles will be announced on separate forms for convenient ordering.

NOTE: To receive up to THREE complimentary copies, check the titles desired and return this entire form to the International Cancer Research Data Bank (ICRDB) Program.*

## CARCINOGENESIS SERIES:

- ☐ The Role of Dietary Nitrate and Nitrite in Human Carcinogenesis (OK-82/01)
- ☐ Age-Related Factors Which May Predispose to Carcinogenesis (OK-82/02)
- ☐ DDT and Its Metabolites in Carcinogenesis (OK-82/03)
- ☐ Polychlorinated Biphenyls and Polybrominated Biphenyls in Carcinogenesis (OK-82/04)
- ☐ Dioxins and Dibenzofurans in Carcinogenesis (OK-82/05)
- ☐ Short-Term Test Systems for Potential Mutagens and Carcinogens: II. Mutagenicity in Mammalian Cell Culture (OK-82/06)
- ☐ Short-Term Test Systems for Potential Mutagens and Carcinogens: III. In Vitro Transformation (OK-82/07)
- ☐ Short-Term Test Systems for Potential Mutagens and Carcinogens: IV. Unscheduled DNA Synthesis (OK-82/08)
- ☐ Short-Term Test Systems for Potential Mutagens and Carcinogens: V. In Vivo Tests for Chromosomal Damage (OK 82/09)
- ☐ Short-Term Test Systems for Potential Mutagens and Carcinogens: VI. In Vitro Tests for Chromosomal Damage (OK-82/10)
- ☐ Selected Enzyme Markers of Hepatocarcinogenesis: Gamma-Glutamyl Transpeptidase, Glucose-6-Phosphatase, Alkaline Phosphatase, ATPase (OK-82/11)
- ☐ Naturally Occurring Dietary Carcinogens of Plant Origin (OK-82/12)
- ☐ Phorbol Ester Action in Cell Culture (OK-82/13)
- ☐ Mutagens and Carcinogens in Cooked, Smoked, and Charred Foods (OK-82/14)
- ☐ Neurocarcinogenesis (OK-82/15)
- ☐ Excision Repair of DNA Damage: I. Enzymology and Mechanisms of Excision Repair (OK-82/16)
- ☐ The Role of Selected Dietary Factors in Carcinogenesis (OK-82/17)
- ☐ Excision Repair of DNA Damage: II. Human Genetic Defects in Excision Repair**
- ☐ Excision Repair of DNA Damage: III. The Regulation of Excision Repair**
- ☐ Chromatin Alterations Associated with Carcinogenesis**
- ☐ Methodology in Use for the Assessment of Carcinogenic Risk: I. Chemical Agents**
- ☐ Methodology in Use for the Assessment of Carcinogenic Risk: II. Radiation**

*Additional titles may be ordered for a small fee from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, Virginia 22161, U.S.A.

**In press - expected in early 1983.

Return this entire form to:

The ICRDB Program
National Cancer Institute
Westwood Building
Room 10A18
Bethesda, Maryland 20205

Print clearly. This will be your mailing label.

Name: _____

Address: _____

_____

_____

**U.S. DEPARTMENT OF COMMERCE**
**National Technical Information Service**
5285 Port Royal Road
Springfield, Va. 22161

OFFICIAL BUSINESS

Penalty for Private Use, $300

**PRINTED MATTER**

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF COMMERCE
COM-211

THIRD CLASS
BULK RATE

U.S.MAIL

CB-17

**CANCERGRAMS** are distributed for the International Cancer Research Data Bank (ICRDB) by the National Technical Information Service (NTIS). **CANCERGRAMS** are available from NTIS on a standing order basis at $2 each for North American Continent addressees and $3 each for other addressees. An NTIS deposit account is required. For a list of subject categories or other information, please write to:

Subscription Section
National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161

**NOTICE OF MAILING CHANGE**

☐ Check here if you wish to discontinue receiving this publication.

☐ Check here if your address has changed and you wish to continue receiving this publication. (Be sure to furnish your complete address including zip code.)

Tear off cover with address label still affixed and send to:

Computer Support Center
ICRDB Program
IIT Research Institute
10 West 35th Street
Chicago IL. 60616